

Chromosomal Basis of Inheritance

Thomas Hunt Morgan

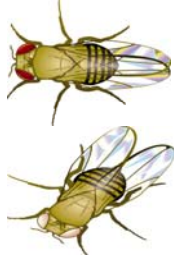
- Performed Experiments and provided convincing evidence for chromosomes.
- Studied *Drosophila*
 - Easy to Culture
 - Breed Extremely fast
 - Short Generation time
 - Four pair of chromosomes that are easily observed in the microscope.

Drosophila

- Three pair of autosomes and one pair of sex chromosomes.
 - Females have two X's
 - Males have an X and Y
 - Wild Type
 - Mutants

Discovery of Sex Linkage

- After an entire year of breeding flies Morgan discovered a white eyed male fly.



Sex Linked Traits

- Sex Linked traits – those that are linked to either the X or y chromosome. Usually the X chromosome
- Eye color was linked to the X chromosome
- Show all crosses

Linked Genes

- Genes on the same chromosome tend to assort together and don't assort independently.
 - When recombination frequency is 50% the two genes are on different chromosomes.
- Linked Genes – On the same chromosome so they tend to be inherited together
- Since they are not separate they will not show a 9:3:3:1 ratio.

Linked Genes

- Show overhead 15.4 Evidence for Linked Genes
- Recombination of Linked Genes
 - Result of Crossing Over.
 - Calculation of Recombination Frequency.

Recombination Frequency

- If wing type and body color were on different chromosomes (unlinked), they would assort independently and show the predicted phenotypes 1:1:1:1.
- If the genes were completely linked, expected results from the test cross would be a 1:1 phenotypic ratio of parental types only.

Recombination Frequency

- Morgan's testcross didn't produce results consistent with linked or unlinked. There was a high percentage of parental phenotypes, which suggested linkage between two genes.
- Morgan found out (discovered) that there must be a mechanism for exchanging parts of chromosomes. Crossing Over.

Recombination Frequency

- b = Black Body b⁺ = Grey Body
- vg = vestigial wings vg⁺ = wild type wings
- + = wild type or most frequently observed.

- Cross grey normal wings with black vestigial

b⁺bvg⁺vg x bbvvgg

Phenotypes	Genotypes	Expected if Unlinked	Expected if Linked	Actual
Black Body, Normal Wings	b vg ⁺	575	1150	206
	b vg	575		965
Grey Body, Normal Wings	b ⁺ vg ⁺	575	1150	944
	b ⁺ vg	575		185
Black Body, Vestigial Wings	b vg	575		
Grey Body, Vestigial Wings	b ⁺ vg			

Calculations

- 2300 total offspring
- 965 and 944 are the same as the parentals
- 206 and 185 are not. Since the majority are like the parents they are probably linked.
- 391/2300 = 17% recombinants.

A.H. Sturtevant

- Student of Morgan.
- Assumed that if crossing over occurs random, the probability of crossing over between two genes is directly proportional to the distance between them.
- He used recombination frequencies to assign them linear position.
 - 1% crossover = 1 map unit =one centimorgan (in honor of Morgan)



Mapping Chromosomes

Loci	Recombination frequency	Approximate Map Units
b vg	17%	18.5 (double crossovers under estimate)
cn b	9 %	9%
cn vg	9.5%	9.5%

Other Types of Mapping

- Linkage Map
 - Based on Cross Over frequencies
- Cytological Maps
 - Locates genes based on chromosomal features like banding pattern etc...
- The ultimate maps are constructed of sequences.

Sex Chromosomes

- Sex Chromosomes vary with organisms.
 - Heterogametic- ie Xy
 - Homogametic - ie XX
- Human
 - XX = 
 - Xy = 

Sex Chromosomes

- What determines male character development?
 - SRY (or Sex-determining region of Y) on the y chromosome triggers a series of events that make testes develop where the ovaries normally do.

Sex Chromosomes

- X linked.
 - Review Color blind crosses
 - Show Pedigree
 - Hemizygous – A condition where only one copy of a gene is present in a diploid organism.
- X inactivation
 - Barr Body

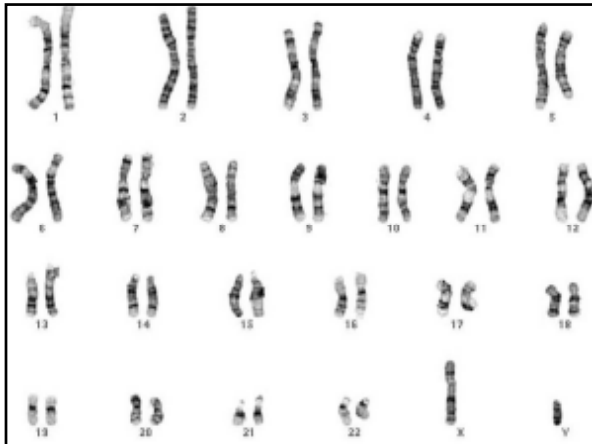
Sex Determination

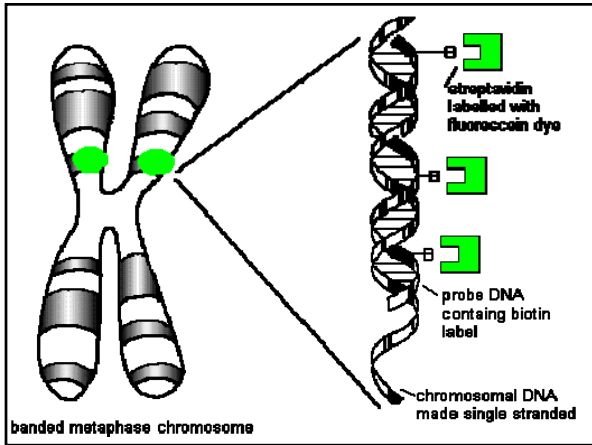
- Mosacism in female X expression
 - Calico cats
 - Sweat gland development
- Barr bodies are highly methylated(XIST gene)
 - Methyl groups attached to cytosine

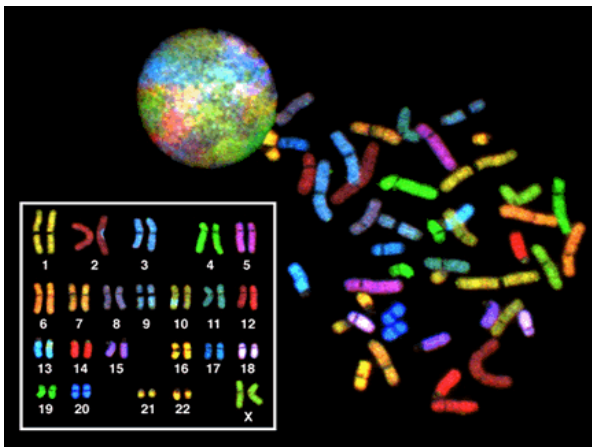
Errors and Exeptions in Chromosomal Inheritance

- Alteration of chromosome number
 - Aneuploid
 - Polyploid
 - All due to non-disjunction
 - either in meiosis one or two
 - What would be the result in mitosis?





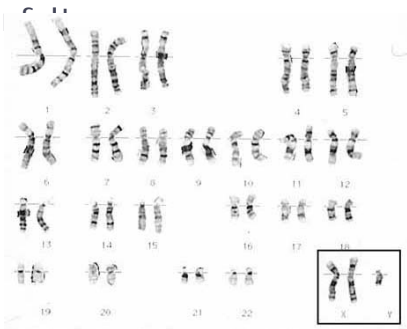




Aneuploidy

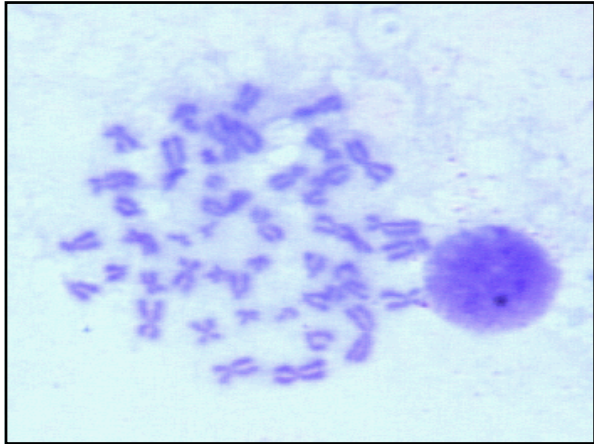
- Condition where there is an abnormal number of certain chromosomes.
 - If there is three it is said to be trisomic.
 - If it is missing one it is said to be monosomic.
 - If there is an error early in development all others will have same problem.
 - There are many symptoms that are a result of aneuploidy. ie Down's Syndrome.

Klinefelter



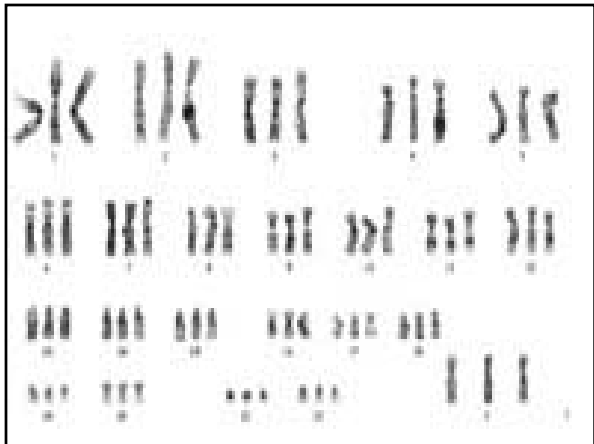
Klinefelters





Polyploidy

- A chromosome number that has more than one complete set of chromosomes.
- Triploidy
- Tetraploidy
- Polyploidy is important in plants.
- Rare in animals, some mosaics occur but very uncommon.



Alteration of Chromosome Structure

- Deletion – loses a piece of a chromosome.
- Fragments without a centromere are usually lost but can attach.
 - Duplication
 - Translocation
 - Inversion
- Crossing over can also cause the same things.
 - Normally reciprocal, but can be non-reciprocal.

Mutations

- Can produce new alleles
 - Must be in the gametes to be passed on
- Types of Mutations
 - Point
 - Can be harmless because of redundancy of code
 - Chromosomal
 - Duplication
 - Inversion
 - Translocation
 - Deletion

Point Mutation and Frame Shift

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Wild type allele:
  N D D Q S R H L Q T L A G V N L
  atggacgatcaatccaggatgctgagactctggccgggtgaacctg

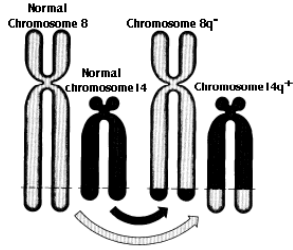
silent (third base pair) mutation:
  N D D Q S R H L Q T L A G V N L
  atggacgatcaatccaggatgctgaaactctggccgggtgaacctg

point mutation (missense):
  N D D Q S R H L K T L A G V N L
  atggacgatcaatccaggatgctgagactctggccgggtgaacctg

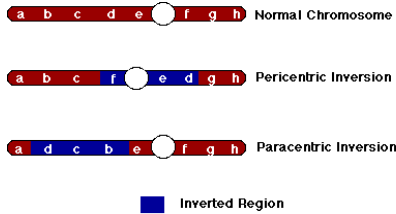
point mutation (nonsense):
  N D D Q S R H L stop
  atggacgatcaatccaggatgctgagactctggccgggtgaacctg

frameshift leading to premature termination:
  N D D Q S R H L R L W P G stop
  atggacgatcaatccaggatgctgagactctggccgggtgaacctg
    
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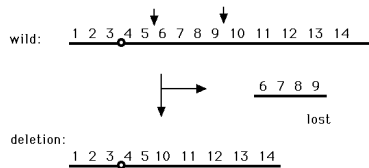
Translocation

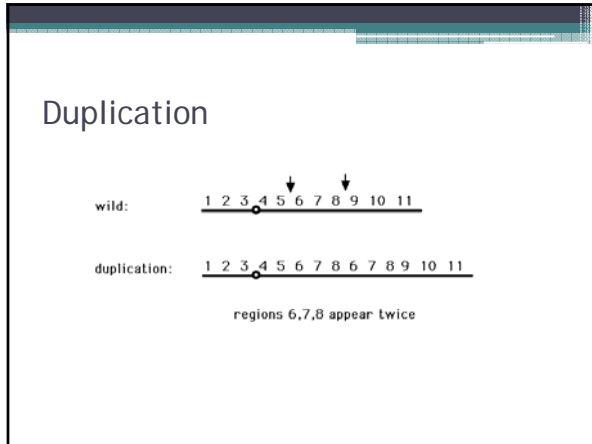


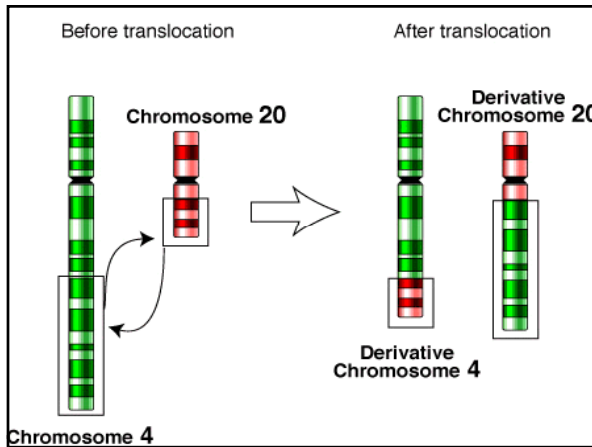
Inversion

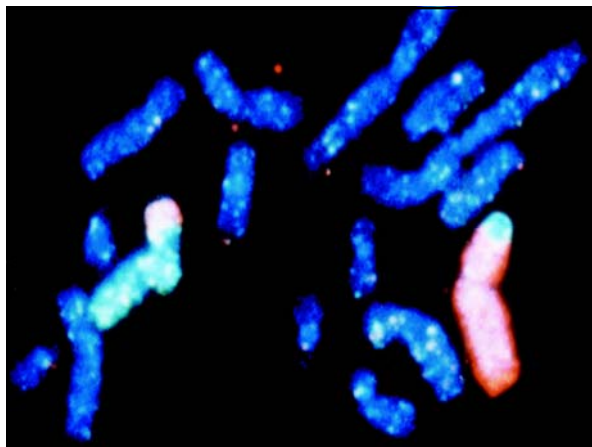


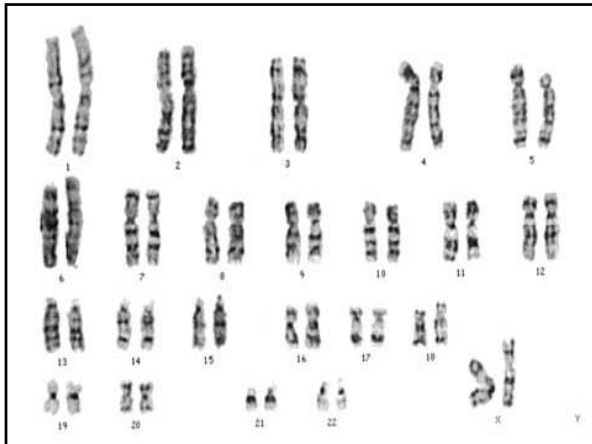
Deletion





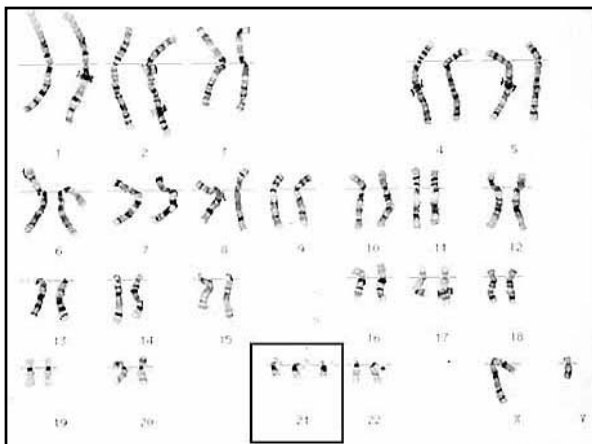


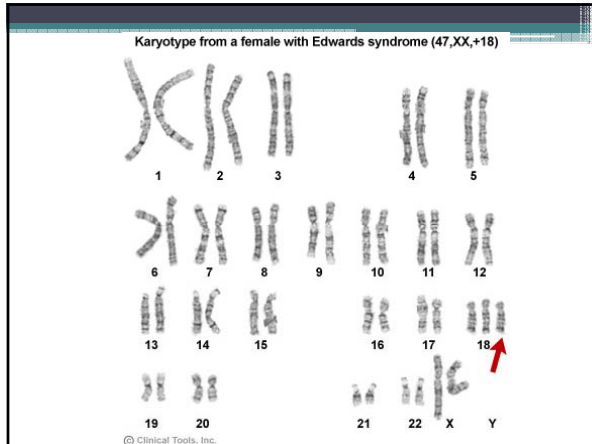




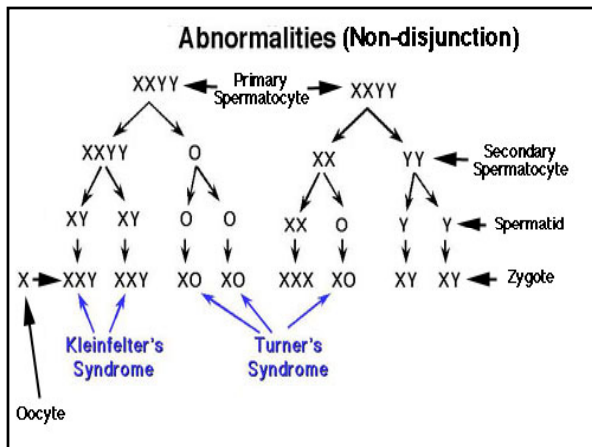
Human Conditions Due to Chromosomal Alteration

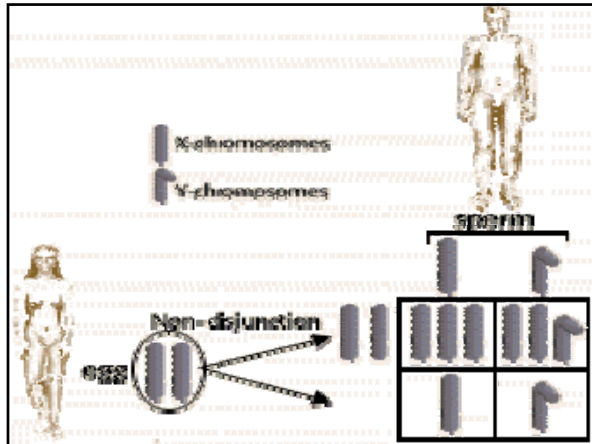
- Down's Trisomy 21
- Patau Syndrome Trisomy 18
- Edwards Syndrome Trisomy 13
- Klinefelter Syndrome XXY
- Extra Y XYY
- Triple X
- Turners XO

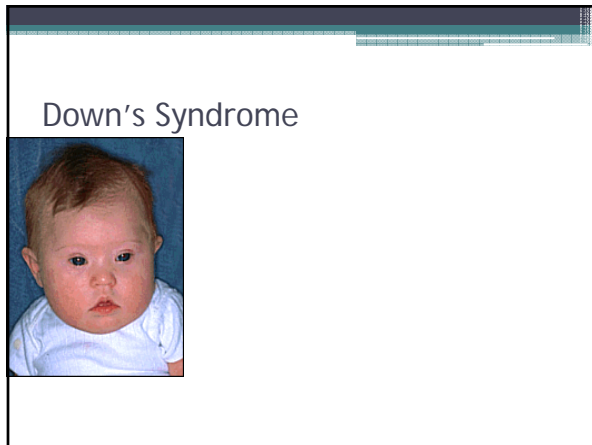












Phenotypes Depend on Who Gives It

- Prader-Willi and Angelman
 - Same deletion on Chromosome 15
 - Paternal gives PW
 - Maternal gives A
 - This is the concept of Imprinted Genes or Genomic Imprinting.
 - Fragile X may be a female imprinted genes

Extranuclear Genes

- Plants get all there Chloroplasts from the egg and none from the pollen.
- Animals get all there mitochondria from the egg and few from the sperm.
