Mendelian Genetics and the Chromosomal Basis for Inheritance

Gregor Mendel began the formal study of genetics.

1866 - showed that inherited factors are passed down unchanged from one generation to the next.
Mendelian Genetics and the Chromosomal Basis for Inheritance

Mendel’s methods were central to his success:

- used pure breeding lines
- made controlled crosses
- followed traits for two generations
- counted many progeny
Cross-pollination

Transfer of pollen with brush

Removal of anthers

Stigma

Progeny

Selfing

Transfer pollen to stigma

Progeny

Figure 2-10
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Monohybrid Cross

Pure breeding lines:
- multiple crosses within strains to insure pure breeding
- controlled crosses between strains
- consistent, repeatable outcomes

Yellow and green peas appear in the $F_2$
6022 yellow, 2001 green = 3:1
Mendel’s discovery led to a genetic hypothesis

Mendel’s results

- Genes are passed down unchanged
- Genes exist as pairs
- Members of pairs separate evenly during gamete formation (Mendel’s 1st law)

Mendel counted the $F_2$ of crosses from seven different traits
Repeateable 3:1 ratios led to three conclusions

Figure 2-12 part 04
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A single gene model explains Mendel’s results

Mendel’s results

- **Pure**: F1
- **Selfed**: F2

Mendel’s explanation

- Passed down unchanged
- Exist as pairs
- Equal segregation

Yellow F2 selfed:
- 1/3 all yellow
- 2/3 yellow, green

Green F2 selfed:
- All green

### Mendel’s results

- **P**: Pure
- **X**: Pure

<table>
<thead>
<tr>
<th>F1</th>
<th>P</th>
<th>Y/Y</th>
<th>y/y</th>
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<tr>
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<td>1/2 Y</td>
<td>1/2 y</td>
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<table>
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*Figure 2-12 part 04
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Mendel needed a direct test of his hypothesis.
F₁ yellow selfed

F₁
- Yellow
- Self-pollinated flowers
- Grow

F₂
- Progeny seeds
- Total 21 7

Test Cross

F₁ yellow × green

F₁
- Yellow
- Grow
- Flowers cross-pollinated
- or
- either

F₂
- Progeny seeds
- Total 11 11
A test cross repeatably produces a 1:1 ratio

Mendel’s results

Test cross: confirmed Mendel’s hypothesis of even segregation
A single-gene model explains Mendel’s ratios

Mendel’s results

Pure

P

×

Pure

F₁

Crossed with green

Selled

1/4

1/2

3/4

F₂

Mendel’s explanation

P Y/Y

× y/y

F₁ Y/y

Equal segregation

× y/y

all y

1/2 Y/Y

1/4 Y/y

1/4 y/y

1/2 y

1/4 Y/y

1/4 y/y

1/2 y

1/4 y/y

1/2 y

1/4 y/y

1/2 y

1/4 y/y

1/2 y

1/4 y/y

1/2 y
A single-gene model explains Mendel’s ratios

Mendel’s results

Pure x Pure

F₁

Selfed

Crossed with green

F₂

Mendel’s explanation

P Y/Y x y/y

F₁ Y/y

Equal segregation

F₂

<table>
<thead>
<tr>
<th>Y/Y</th>
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<td>1/2</td>
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</table>

Figure 2-12 part 15
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Summary of Mendel’s Results

### Monohybrid Cross

**Yellow** ⋀ **green**

<table>
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<th>Outcome</th>
<th>Gametes</th>
<th>Genotypes</th>
<th>Color</th>
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<td>½Y, ½y</td>
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<td>YY ⋄ Yy ⋄ yY ⋄ yy</td>
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<td></td>
<td></td>
<td>yy</td>
<td>green</td>
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### Test Cross

**Yellow** ⋀ **green**

<table>
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<th>Genotypes</th>
<th>Color</th>
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</tr>
<tr>
<td>F2</td>
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<td>Yy ⋄ yy</td>
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<td>1/2 Yy, Yellow</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>1/2 yy, green</td>
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</tr>
</tbody>
</table>

Demonstrates even segregation of alleles
The chromosomal basis for Mendel’s law of segregation:

Genes are located on chromosomes – two copies of each in each diploid cell (homologs)

Even separation of homologs during meiosis causes even separation of alleles
Molecular Alleles follow Mendelian Inheritance

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Many organisms:
• dominant phenotype = \( C \), active allele, expression+
• recessive phenotype = \( c \), inactive allele, expression-

Microorganisms:
• wildtype = \( bio^+ \), active allele
• mutant = \( bio^- \), inactive or null allele

*Drosophila*:
• recessive mutation = \( bw \), wildtype allele = \( bw^+ \)
  • recessive mutation is loss of function or null
• dominant mutation = \( Cy \), wildtype allele = \( Cy^+ \)
  • dominant mutation is gain of function
A white eyed mutant male was discovered in a wildtype culture – 1910, Thomas and Lilian Morgan
Inheritance of white eyes in *Drosophila* does not follow expected Mendelian patterns.

Inheritance patterns differ between the sexes.
Inheritance of white eyes

white eyed mutant male ♂ red eyed female

\[
F_1 = \text{all red eyed}
\]

\[
F_2 = \frac{3}{4} \text{ red eyed, } \frac{1}{4} \text{ white eyed}
\]

except that – males = \(\frac{1}{2}\) red, \(\frac{1}{2}\) white
females all red eyed

The reciprocal cross:

white eyed female ♀ red eyed male

\[
F_1 = \text{all females red eyed, males white eyed}
\]

\[
F_2 = \text{males and females both } \frac{1}{2} \text{ red, } \frac{1}{2} \text{ white}
\]
Inheritance of Sex Chromosomes

Autosomes: one pair of each in male and female

Sex chromosomes:
- male: X, Y
- female: X, X

Inheritance of sex chromosomes explains the inheritance of white eyes
Inheritance of white eyes

white eyed male (XY) $\times$ red eyed female (XX)

$F_1 = \text{all red eyed (XX, XY)}$

$F_2 = 3/4 \text{ red eyed, 1/4 white eyed}$

females all red eyed (XX, XX)

males = 1/2 red (XY), 1/2 white (XY)

The reciprocal cross:

white eyed female (XX) $\times$ red eyed male (XY)

$F_1 = \text{females red eyed (XX)}$

males white eyed (XY)

$F_2 = \text{males and females both 1/2 red, 1/2 white (XY, XY; XX, XX)}$
Chromosomal Basis for X-linked inheritance

**First cross**

P

\[ \text{w}^+ \text{X X} \times \text{w} \text{X Y} \]

Red female

White male

F1

Male gametes

\[ \frac{1}{2} \text{w}^+ \text{ Male gametes} \]

\[ \frac{1}{2} \text{w} \text{ Male gametes} \]

Female gametes

\[ \frac{1}{2} \text{w}^+ \text{ Female gametes} \]

\[ \frac{1}{2} \text{w} \text{ Female gametes} \]

1 Red female

1 Red male

F2

Male gametes

\[ \frac{1}{2} \text{w}^+ \text{ Male gametes} \]

\[ \frac{1}{2} \text{w} \text{ Male gametes} \]

Female gametes

\[ \frac{1}{4} \text{w}^+ \text{ Female gametes} \]

\[ \frac{1}{4} \text{w} \text{ Female gametes} \]

1 Red female

1 Red male

\[ \frac{1}{2} \text{w}^+ \text{ Female gametes} \]

\[ \frac{1}{2} \text{w} \text{ Female gametes} \]

1 White female

1 White male

Figure 2-19 part 2

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Chromosomal Basis for X-linked inheritance

Second cross

P

\[
\begin{array}{c}
w \hspace{1cm} w \\
X \hspace{1cm} X \\
\text{White female}
\end{array}
\hspace{2cm}
\begin{array}{c}
w^+ \\
X \hspace{1cm} Y \\
\text{Red male}
\end{array}
\]

\[\times\]

F₁

\[
\begin{array}{c|c|c}
& w^+ & w \\
\hline
w & \frac{1}{2} & \frac{1}{2} \\
& w^+ \hspace{1cm} w & \\
\hline
\frac{1}{2} \text{ female} & \frac{1}{2} \text{ male}
\end{array}
\]

F₂

\[
\begin{array}{c|c|c|c|c}
& w & w^+ & w & w \\
\hline
w & \frac{1}{2} & \frac{1}{2} & \frac{1}{4} \text{ female} & \frac{1}{4} \text{ male} \\
& w^+ & w & w & w \\
\hline
\frac{1}{2} \text{ female} & \frac{1}{2} \text{ male}
\end{array}
\]

Male gametes

Female gametes
Inheritance of white eyes

white eyed male \((X^w Y) \otimes\) red eyed female \((X^{w+} X^{w+})\)

\[F_1 = \text{all red eyed} \ (X^{w+} Y, X^{w+} X^w)\]

\[F_2 = \frac{3}{4} \text{red eyed, } \frac{1}{4} \text{white eyed}\]

- females all red eyed \((X^{w+} X^{w+}, X^{w+} X^w)\)
- males = \(\frac{1}{2} \text{red} \ (X^{w+} Y), \frac{1}{2} \text{white} \ (X^w Y)\)

The reciprocal cross:

white eyed female \((X^w X^w) \otimes\) red eyed male \((X^{w+} Y)\)

\[F_1 = \text{females red eyed} \ (X^{w+} X^w)\]

- males white eyed \((X^w Y)\)

\[F_2 = \text{males and females both} \ 1/2 \text{red, } 1/2 \text{white} \ (X^{w+} Y, X^w Y; X^{w+} X^w, X^w X^w)\]
Mendelian inheritance can be studied in humans by analyzing pedigrees.
Inheritance of Brown Hair Color

- Mahogany
- Swedish blonde
- Ebony
- Oak
- Honey
- Blonde

Legend:
- Male
- Female

Hair Color (shade of brown):
- Ebony
- Mahogany
- Oak
- Honey
- Blonde

Diagram represents the genetic inheritance pattern for brown hair color.
Rare recessives may become homozygous due to inbreeding
Genotypes may be inferred from inheritance patterns

Figure 2-29 part 11
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Inheritance of an autosomal dominant character
Inheritance of a rare X-linked character
Inheritance of a rare X-linked character

Outside of line, Unlikely to carry allele (be heterozygous)
Inheritance of a rare X-linked character

Figure 2-28
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X-linked recessive traits are much more common in males than females:

Red-green colorblindness: about 8% males and 0.5% females of northern European ancestry

Explanation:

$X^c$ frequency = 8% = 0.08, $X^c = 92\% = 0.92$

Males: one $X^c$ needed for color blindness

$X^cY = 8\%, X^cY = 92\%$

Females: two $X^c$ needed for color blindness

$X^cX^c = 0.08 \times 0.08 = 0.006, \approx 0.5\%$
How to Characterize Genes by Inheritance Patterns in Pedigrees

• First, dominant or recessive?
  • A trait is recessive if there is any case of two unaffected parents producing at least one affected child – if not, consider it dominant.
  • A recessive trait will usually be rare overall, a dominant trait will be common in some lineages, absent in others.
How to Characterize Genes by Inheritance Patterns in Pedigrees

• Second, autosomal or X-linked?
  • A recessive X-linked trait will be much more common in males than in females – else autosomal.
    • Also, affected females must have affected fathers.
  • A dominant X-linked trait will be passed from an affected father to all daughters and no sons.
Pedigrees can help estimate the chance of having affected children
Pedigrees can help estimate the chance of having affected children
Molecular Alleles follow Mendelian Inheritance
Genomic Organization:
Life on earth exhibits a wide range of chromosome and genetic organization:

Viruses - small genomes, simple organization, DNA or RNA, typically linear
NASA: “Life is a self-sustained chemical system capable of undergoing Darwinian evolution.”

Life is defined through its metabolism and ability to reproduce itself and evolve.
Prokaryotic genomes are larger, more complex

*E. coli*: 4600 kb, ~4300 genes

*F* plasmid: 100 kb, ~100 genes
Inheritance occurs during cell division
Prokaryotic cells divide by binary fission

Rod-Shaped Bacterium, hemorrhagic *E. coli*, strain 0157:H7 (division) (SEM x22,810). This image is copyright Dennis Kunkel at [www.DennisKunkel.com](http://www.DennisKunkel.com)
Eukaryotes have multiple genomes

**Eukaryotic cell**

- **Mitochondrial chromosome**
  - Human mt: 16 kb, 37 genes

- **Nuclear chromosomes**
  - 120-160 kb, 100+ genes

- **Chloroplast chromosome (plants)**

**Human nuclear**
- 3000 mbp, 21k genes

**DNA-protein supercoil**

**Figure 1-14 part 1**
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Genomic Structure in Different Organisms: simpler organisms → smaller genomes, relatively more coding and less noncoding DNA

**Bacterium** 13 genes / 20 kb

**Yeast** 11 genes / 20 kb

**Drosophila** 0.8 genes / 20 kb

**Human** 0.33 genes / 20 kb

Total coding DNA per segment
Eukaryotic Genome Comparison

- **Baker’s Yeast (S. cerevisiae):** microscopic
  - 12,200 kb, ~6,000 coding genes,
  - 73% coding
- **Nematode (C. elegans)** 1 mm long, 1,000 cells:
  - 100,000 kb, ~19,000 coding genes
  - ~28% coding
- **Drosophila melanogaster**
  - 140,000 kb, ~17,000 coding genes
  - ~18% coding
- **Humans**
  - 3,100,000 kb, ~21,000 coding genes
  - <2% coding
Organization of Eukaryotic Chromosomes

DNA + histones = chromatin

Human Nucleus:
0.006 mm diameter
2,000 mm DNA

Equivalent:
40 km fine thread
into a tennis ball
Another Representation of a Nucleosome - Crystal Structure
Eukaryotic DNA - histones removed

Scaffold
Both Prokaryotic and Eukaryotic Chromosomes are Mounted on Scaffolds
Eukaryotic somatic cell division: mitosis + cytokinesis
Formation of identical daughter cells

Mitosis in a haploid eukaryotic cell

- Interphase
  - G1
  - S
  - G2
- Mitosis
- Nucleus
- n
- M
- n
- Identical haploid daughter cells

Mitosis in a diploid eukaryotic cell

- Interphase
  - G1
  - S
  - G2
- Mitosis
- 2n
- 2n
- Identical diploid daughter cells
Prokaryotic / Eukaryotic Chromosomes and Cell Reproduction

**Prokaryotes**
- Chromosome continuous
- Introns lacking
- Intergenic spacers lacking
- DNA “naked”
- Binary fission

**Eukaryotes**
- Chromosomes linear
- Introns usually present
- Intergenic spacers present, may be large
- DNA bound with histone proteins
- Mitosis + cytokinesis
Mitosis: asexual transmission of genetic information
Mitosis results in even distribution of replicates to daughter cells.

- **G₀** - cell specialization, no more divisions (2c, 2n)
- **Interphase G¹** (2c, 2n)
- **Interphase S** (2c × 2 = 4c, 2n)
- **Prophase** (4c, 2n)
- **Cytokinesis** (2c, 2n) (2c, 2n)
- **Metaphase** (4c, 2n)
- **Anaphase** (2c × 2, 2n × 2)
- **Telophase** (2c × 2, 2n × 2)

**Mitosis** is a cycle.
Human chromosomes are best visualized at mitotic metaphase.

Coiling and folding during prophase results in about a 7,500 fold reduction in length of human chromosomes (45mm to < 0.006 mm).
Organization of genes on chromosome 22 the second smallest autosome

(A) human chromosome 22 in its mitotic conformation, composed of two DNA molecules, each $48 \times 10^6$ nucleotide pairs long

(B) 10% of chromosome arm ~40 genes

(C) 1% of chromosome containing 4 genes

(D) one gene of $3.4 \times 10^4$ nucleotides:
- regulatory DNA sequences
- exon
- intron
- gene expression
- protein
- folded protein
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<tr>
<td>Y</td>
<td></td>
<td></td>
<td>2.2 (group G)</td>
<td>27 (A)</td>
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*Black dot indicates position of centromere on length of chromosome.

†Percentage of the total combined length of a haploid set of 22 autosomes.

‡Percentage of chromosome’s length spanned by its short arm. The four most metacentric chromosomes are indicated by an (M), the four most acrocentric by an (A).
Human Female Karyotype
Human Male Karyotype
Ideograms are used to depict chromosome banding.

Light bands = euchromatin (active genes)
Dark bands = heterochromatin (~inactive)
Chromosome ideograms may show different resolution.
Chromosomes can be stained using fluorescent probes.
Genes can be located on human mitotic metaphase chromosomes using fluorescent probes
Genes can be located on human mitotic metaphase chromosomes and mapped to a specific region using fluorescent probes.

The EMBO Journal (1997) 16, 1093 - 1102
doi:10.1093/emboj/16.5.1093
Mitotic chromosomes at the same scale

Region where homologues have separated

Chromosome 3 right arm

X chromosome

Normal mitotic chromosomes at the same scale

Region where the two homologous chromosomes are separated

Chromocenter

Chromosome 4

Chromosome 3 left arm

Chromosome 2 left arm

Chromosome 2 right arm

20 µm
A diagram of *Drosophila buzzatii* polytene chromosomes
Labeled DNA probes can be used to locate genes on polytene chromosomes.
Eukaryotic sex cell division: meiosis + cytokinesis
Formation of haploid cells from diploid parents
Meiosis I:
- Replication
- Homologs separate

Meiosis II:
- Replicates (chromatids) separate

Processes:
- Interphase
- Prophase I
- Metaphase I
- Anaphase I
- Telophase I
- Prophase II
- Metaphase II
- Anaphase II
- Telophase II

Products of meiosis: $n$
meiosis is not a cycle

Crossing over
Meiosis: Stages of Prophase I under a microscope

- Leptotene: thin thread
- Zygotene: paired thread
- Pachytene: thick thread
- Diplotene: double thread
CROSSING OVER

X-overs hold chromatids together

paternal sister chromatids
chromatid 1
chromatid 2
chromatid 3
chromatid 4

maternal sister chromatids

assembling central region of synaptonemal complex

INTERPHASE

ZYGOTENE

DIPLOTENE FOLLOWED BY DIAKINESIS

Synaptonemal complex

(A) chiasma

(B)

(C) studyblue.com
Meiosis: Stages of Prophase I

- **Leptotene** – thin thread
- **Zygotene** – paired thread
- **Pachytene** – thick thread
- **Diplotene** – double thread
- **Diakinesis** – moving through
- **Chromosomes pair**, beginning at the telomeres
- **Synapsis** occurs with the formation of the synaptonemal complex.
- **Crossing over** occurs – required (~) for proper alignment at metaphase
- **Synaptonemal complex** dissolves, homologs repel
- **Chiasmata** appear
- **Crossovers** terminalize (during anaphase)
Chromosomal effects of prophase I:

- alignment, segregation of homologs
- chromosomal recombination

Genetic effects:

- even segregation of alleles
- genetic recombination
Human (and Mammalian) Meiosis

Males –
  • Meiosis begins about puberty
  • Initial wave of meiosis takes about 2 months to complete
  • Subsequent meiosis is a continuous process throughout the life of the individual

Females –
  • Prophase I begins at ~10 weeks gestation
  • At diplotene (~26 weeks) meiosis is arrested until puberty
  • At puberty, meiosis proceeds to metaphase II, where it is arrested until fertilization
  • Meiosis is completed upon fertilization
Sex Chromosomes

X and Y are different over most of their sequence, but pair during meiosis in a pseudoautosomal region that is homologous and contains equivalent genes.

[Diagram showing the pairing regions of X and Y chromosomes in Homo sapiens and Melandrium album]
Sex Determination

• XY – male is the heterogametic sex
  • Humans: Y determines sex by action of *SRY* (sex determining region)
  • Drosophila: X:autosome ratio determines sex, genes on Y determine male fertility
• ZW – female is the heterogametic sex
  • Birds, some moths and butterflies, some reptiles
• No sex chromosomes
  • Crocodiles and alligators
  • Developmental temperature determines sex
    • 80-85°C F, mostly female
    • 90-95°C F, mostly male
Human X
about 153 mb, 2000 genes

Human Y
about 55 mb, 90 genes
- mostly heterochromatin
- evolved from X

X-linked genes potentially imbalanced between sexes

One X in each adult female cell is inactivated

X-inactivation provides equal “doses” of X-linked gene products for male and female - gene dosage compensation
Mary Lyon 1961: Barr bodies represent inactivated X chromosomes
There is a direct association between the number of X chromosomes and the number of Barr bodies.

Hong B et al. PNAS 2001;98:8703-8708
Enzymes and DNA often have allelic differences that allow them to be separated by electrophoresis.

Electrophoretic alleles may be referred to as “fast” or “slow”.

For X-linked genes, all males and all homozygous females show only fast or slow bands. Heterozygous females show both.
Glucose-6-phosphate dehydrogenase (G6PD):
X-linked gene involved in glycolysis, protection of red blood cells from oxidizing free radicals
Electrophoretic variants exist that have little or no effect on health
G6PD Variation - DNA Electrophoresis

Mark
Fast
Fast
Slow
F/S
Mark

100 bp
25 bp

Burgoiné, K. L. et al. 2010 Malaria Journal V9-1
DOI: 10.1186/1475-2875-9-376
Electrophoretic Pattern

Genotype of Individual

Well

Slow

Fast

$X^fY$  $X^sY$  $X^fX^f$  $X^sX^s$
Heterozygous Female
Random Cells

Electrophoretic Pattern

Well

Slow

Fast

Genotype of Individual

$X^fY$  $X^sY$  $X^fX^f$  $X^sX^s$  $X^fX^s$  $X^fX^s$
Heterozygous Female
Random Cells

Clonal Colonies from
Individual Cells

Electrophoretic Pattern

Well

<table>
<thead>
<tr>
<th>Slow</th>
<th>Fast</th>
</tr>
</thead>
<tbody>
<tr>
<td>X_fY</td>
<td>X_sX_f</td>
</tr>
<tr>
<td>X_fX_f</td>
<td>X_sX_s</td>
</tr>
<tr>
<td>X_fX_s</td>
<td>X_fX_s</td>
</tr>
</tbody>
</table>

Genotype of Individual
Heterozygous Female
Random Cells

Clonal Colonies from
Individual Cells

Electrophoretic Pattern

Well

Slow

Fast

Genotype of Individual

$X^f Y$

$X^s Y$

$X^f X^f$

$X^s X^s$

$X^f X^s$

$X^f X^s$

$X^f X^s$

$X^f X^s$

$X^f X^s$

$X^f X^s$
X inactivation explains female mosaicism for X-linked genes
**X chromosome inactivation**

$X^B = \text{orange}$  
$X^b = \text{non-orange}$  
$X = \text{black}$

**Zygote**

**Early Divisions**

**Random Inactivation**  
($\sim 20$ cell stage)

**Expression of $Xist$**

Inactivated $X$ passed to all somatic descendants  
$\rightarrow \text{somatic mosaicism}$

$X$ reactivated during oogenesis
Summary:

Males, homozygous females are orange or black

Random X inactivation in heterozygous females produces mosaics.

$X^B =$ orange
$X^b =$ non orange
$= $ black

http://www.bio.miami.edu/dana/dox/calico.html
Changes in Chromosome Number

Euploidy: increase or decrease in the entire genome
- Monoploidy - single chromosome set (2n to n)
- Polyploidy - multiple chromosome sets
  - Example: 2n to 4n, 4n to 8n, 3n to 6n

Chromosomes from http://en.wikipedia.org/wiki/Polyploid
Changes in Chromosome Number

Euploidy: increase or decrease in the entire genome
– Monoploidy - single chromosome set (2n to n)
– Polyploidy - multiple chromosome sets
  – Example: 2n to 4n, 4n to 8n, 3n to 6n

• allopolyploid - chromosome sets from different species
  – results from polyploidy in a sterile monoploid hybrid
• autopolyploid – chromosome sets from same species (most common)
  – produces a new tetraploid species not interfertile with parent
Male donkey ♀ female horse = mule (sterile)
\[2n = 62 \quad 2n = 64 \quad n = 31 + 32 = 63\]

Male lion ♂ female tiger = liger (partially fertile)
\[2n = 38 \quad 2n = 38 \quad n = 19 + 19 = 38\]
Autopolyploids:
- a new tetraploid species
- cannot interbreed with the parent species
  - sterile triploids result from interbreeding
Self Fertile Ancestral

Diploid (2N)

Self Fertile Derived

Tetraploid (4N)

Gametes

Haploid (N)

Gametes

Diploid (2N)

Triploid (3N)

Sterile Triploid

Chromosomes from http://en.wikipedia.org/wiki/Polyploid
Basis for sterility of triploids: meiosis produces gametes with uneven numbers of chromosomes
Trivalents (or bivalents and univalents) form during metaphase I.

Chromosomes from http://en.wikipedia.org/wiki/Polyploid
Trivalents (or bivalents and univalents) form during metaphase I and segregate unevenly during anaphase.
Telophase I daughter cells have unbalanced chromosome numbers.

Chromosomes from http://en.wikipedia.org/wiki/Polyploid
Final distribution of chromosomes in gametes: uneven number leads to inviability

Chromosomes from http://en.wikipedia.org/wiki/Polyploid
Changes in Chromosome Number

Aneuploidy

Aneuploidy is an increase or decrease in number for a single chromosome, all others stay the same.

Monosomy (one copy)

Trisomy (three copies)

Chromosomes from http://en.wikipedia.org/wiki/Polyploid
Aneuploidy results from nondisjunction - chromosomes do not segregate normally.

Nondisjunction produces uneven distribution of chromosomes in gametes.

Nondisjunction in meiosis I is more common due to sensitivity of crossing over.
Aneuploidy: change in number for a single chromosome

• Sex chromosome aneuploidy
  – monosomy = one copy of the X chromosome
    • X is the only monosomic that can survive
    • XO, Turner syndrome
  – trisomy = three copies of sex chromosome
    • XXY, Klinefelter Syndrome
    • XYY, Jacob Syndrome
    • XXX, triplo X female, generally asymptomatic
Human sex chromosome aneuploidy – Turner and Klinefelter Syndrome
Turner Syndrome

- Short stature
- Low hairline
- Shield-shaped thorax
- Widely spaced nipples
- Shortened metacarpal IV
- Small fingernails
- Brown spots (nevus)
- Characteristic facial features
- Fold of skin
- Constriction of aorta
- Poor breast development
- Elbow deformity
- Rudimentary ovaries
- Gonadal streak (underdeveloped gonadal structures)
- No menstruation

Conceptions:
13,580/1,000,000
Survive – 80
Spontaneously abort - 13,500
Klinefelter Syndrome

Conceptions: 480/1,000,000
Survive - 440
Spontaneously abort - 40

Figure 16-15
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Akhenaten
Amenhotep IV
XXY?

DNA evidence says not
Jacob or XYY Syndrome

- Occurrence, survival ≈ Klinefelter syndrome
- Slightly taller than average
- Increased risk of learning disabilities, no significant effect on IQ
- Development of speech language and motor skills may be delayed
- Normal sexual development and usually normal fertility
- No increase in aggression

The XYY Factor: How a rare chromosome disorder . . .

One mother’s account of having an XYY son.  
http://www.dailymail.co.uk/health/article-1082293/The-XYY-Factor-How-rare-chromosome-disorder-brought-son-world-pain.html#ixzz2fqVy3IJi
Human Autosomal Trisomy
Trisomics that may survive to birth are circled
Three Surviving Autosomal Trisomics

• Trisomy 13, Patau Syndrome
  • 12% survive to birth
  • 130 day life expectancy, >80% die within 1 year

• Trisomy 18, Edward Syndrome
  • 6% survive to birth
  • 50% die within 1 week, rarely live to teens
    • Survivors have serious medical and developmental problems

• Trisomy 21, Down Syndrome – the most common
  • 25% survive to birth
  • Life expectancy variable, 8% live past 40
  • Substantial medical intervention, parental care likely
    • Low IQ (mean 50), heart disease, vision/hearing disorders common
Down Syndrome

Growth failure
Mental retardation
Flat back of head
Abnormal ears
Many "loops" on fingertips
Palm crease
Special skin ridge patterns
Unilateral or bilateral absence of one rib
Intestinal blockage
Umbilical hernia
Abnormal pelvis
Diminished muscle tone

Broad flat face
Slanting eyes
Epicanthic eyefold
Short nose
Short and broad hands
Small and arched palate
Big, wrinkled tongue
Dental anomalies
Congenital heart disease
Enlarged colon
Big toes widely spaced

Conceptions:
4,551/1,000,000
Survive – 1041
Abort – 3510

Figure 17-16
Introduction to Genetic Analysis, Tenth Edition
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Amniocentesis & Chorionic Villus Sampling

(a) Amniocentesis

Ultrasound scanner
Placenta
Amniotic fluid
Fetus
Uterus
Catheter

(b) Chorionic villus sampling

Ultrasound scanner
Uterus
Embryo
Chorion

Incidence of Down syndrome per number of births

0 20 25 30 35 40 45

1/2300 1/1600 1/1200 1/880 1/290 1/100 1/46

Age of mother (years)

Figure 16-17
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**Aneuploidy**

<table>
<thead>
<tr>
<th>Aneuploidy</th>
<th>Total</th>
<th>Live</th>
<th>Abort</th>
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</thead>
<tbody>
<tr>
<td>XO</td>
<td>13580</td>
<td>80</td>
<td>13500</td>
</tr>
<tr>
<td>XYY</td>
<td>500</td>
<td>460</td>
<td>40</td>
</tr>
<tr>
<td>XXY</td>
<td>480</td>
<td>440</td>
<td>40</td>
</tr>
<tr>
<td>Tri 21</td>
<td>4551</td>
<td>1041</td>
<td>3510</td>
</tr>
<tr>
<td>Tri 18</td>
<td>2360</td>
<td>130</td>
<td>2230</td>
</tr>
<tr>
<td>Tri 13</td>
<td>1450</td>
<td>170</td>
<td>1280</td>
</tr>
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</table>