Animal life cycle

- 1n haploid gametes have 1 set of chromosomes
- 2n diploid zygote has 2 sets of chromosomes

Homologous chromosomes
1 pr sex chromosomes
22 prs. autosomes
KARYOTYPE

1. Obtain white blood cells from or fetal cells from amniotic fluid
2. Proliferation via growth factor add colchicine at metaphase to arrest spindle formation
3. add water to swell cell -> squash
4. stain -> photograph

Detects number of chromosomes, sex, chromosomal abnormalities
Pig karyotype
Arrange in pairs according to:

- decreasing size
- centromere position
- banding pattern
metacentric (1) submetacentric (9)

p arm is the upper, shorter arm
Normal male

46, XY

Which are meta-, submeta- acrocentric?
Do more chromosomes mean more intelligence?

<table>
<thead>
<tr>
<th>Species</th>
<th>Chromosomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human</td>
<td>46</td>
</tr>
<tr>
<td>Chimpanzee</td>
<td>48</td>
</tr>
<tr>
<td>Dog</td>
<td>78</td>
</tr>
<tr>
<td>Cat</td>
<td>72</td>
</tr>
<tr>
<td>Alligator</td>
<td>32</td>
</tr>
<tr>
<td>Goldfish</td>
<td>94</td>
</tr>
<tr>
<td>Mosquito</td>
<td>6</td>
</tr>
<tr>
<td>Potato</td>
<td>48</td>
</tr>
<tr>
<td>Baker’s yeast</td>
<td>34</td>
</tr>
</tbody>
</table>
Chromosome Theory of Inheritance

- 1902 Sutton and Boveri
  - A chromosome is a linkage group of Mendelian factors (GENES)
  - How many linkage groups in the human species?

- 1920s Morgan et al.
  - Genes are in a linear sequence on the chromosomes, they can be mapped
Sex chromosomes

1 pair sex chromosomes

XY heterogametic
XX homogametic
X-linked traits
Genetics Home Reference page (National Library of Medicine)

- Collagen
- Blood clotting factor
- Red blood cell enzyme
- Dystrophin muscle protein
- Color vision gene
Human Male hemizygous for X-linked traits

$X^H Y$

$X^h Y$
- **Human Female = XX**
  - two alleles for each X-linked gene
  - dominance
  - $X^H X^H$
  - $X^H X^h$
  - $X^h X^h$
X-linked genes

- Hemophilia (recessive) 1/5000 males
  - Mutation in gene for clotting factor

Xq28
Occurrence of hemophilia in royal families of Europe

• Mate IV 2 with homozygous normal female p(hemophilia)?
• Mate III 13 with III 1 Probability of offspring?

Criss cross inheritance of X linked traits
Fruit fly nomenclature  box 12.1

Red eyes is wildtype phenotype, brown is mutant
bw+ = wildtype allele
bw = brown allele

*genotype*  *phenotype*

red  brown
- Wingless is recessive mutant (wg allele)
- Genotype of wildtype, heterozygote, mutant?
A white-eyed female is crossed with a red-eyed male. An F1 female from this cross is mated with her father and an F1 male is mated with his mother. What will be the eye color of the offspring of these two crosses?
Mammalian sex determination = the Y system

A. Embryo is neither male nor female

Week 7

How does embryo “know to become male?”
XY embryo sex chromosomes

- The Y determines sex
B. SRY gene encodes TDF

- **SRY (sex determining region Y)**
- p arm
- Gene TDF encode 20 aa transcription factor
- Expression stimulates growth of testes →
- Testosterone ---→ sperm ducts, male brain “sensitization”
6th week of pregnancy

Figure 10-2

Precursor of female internal sex organs (Müllerian system)

Precursor of male internal sex organs (Wolffian system)

Immature gonad

Early in Fetal Development

Sperm

Ovum

Ovum

Sperm

Zygote

Zygote

TDF

Indifferent gonads

No TDF

Testes

Seminiferous tubules

Develop in early embryo

Interstitial cells

(Follicles do not develop until third trimester)

Ovaries
- Sex of 45, XO? (Turner syndrome)
- Sex of 47, XXY? (Klinefelter syndrome)
- Non-disjunction during meiosis
Clinical application

During sperm formation: SRY crossed over to X chromosome

X containing sperm fertilized egg

Child?
Clinical application

- 17 year old female presented with streak ovaries, no uterus
- Karyotype is XY
3. Experiments with transgenic mice

XX males

Add SRY DNA to female mouse embryo
Pseudoautosomal region of the X and Y

- ~12 genes on X and Y
- regions allow X and Y to pair during meiosis

- pseudoautosomal genes are also transcribed from the inactivated X!
- both males and females have 2 active copies of these genes
Dosage Compensation (mammals)

- Females have 2 Xs, males have 1 X. Do females have an extra dose of X-linked genes/alleles?
X chromosome inactivation  Lyon, 1961

- Dense “Barr body” at edge of nucleus in female cells

Number of X chromosomes?
Random X-inactivation

Epigenetic silencing of 1 X chromosome
Random
1000 cell embryo (16 day old in humans)
XIC, Xist gene on X chromosome
transcribed 24 hours prior to inactivation
mRNA “cages” X-chromosome  \( \rightarrow \) becomes a Barr body

Embryo develops patches

Barr body

mRNA
Female mosaics

- Females heterozygous for X-linked traits are mosaics for those traits.

  red/green colorblindness $X^C X^c$

  phenotype = ?
Genesis of a Tortiseshell Cat

One-cell Embryo

Multicellular Embryo

X with orange allele

X with black allele

Inactivated X

X inactivation

Clones of cells represented in skin
Anhydrotic ectodermal dysplasia

$X^A X^a$ female

What happens to $X^a Y$?
Other sex determination systems

A. Drosophila

Ratio of X to sets of autosomes

The Y is not related to sex

\[ \frac{X}{A} = 1 \text{ or } >1 \rightarrow \text{female} \]

\[ \frac{X}{A} = 0.5 \text{ or } <0.5 \rightarrow \text{male} \]

\[ \frac{X}{A} \text{ between } 0.5 \text{ and } 1 \rightarrow \text{intersex} \]

Sex of an XY fly with 2 sets of autosomes?

Sex of a fly with with 2 sets of autosomes, 1 X chromosome

Sex of a triploid fly with 2 X chromosomes?
ZW system - birds

- Females ZW (heterogametic)
- Males ZZ (homogametic)

Barred feathers is Z-linked and a dominant allele

A male with non-barred feathers is crossed to a female with barred feathers.

Allele key:
All female offspring?
Temperature sex determination (TSD)

- In some reptiles sex is not determined genetically
- Turtles – if T is cool → all male offspring
- Crocodile - low and high T → all female
- Some reptiles have XY system, some ZW
Parthenogenesis – eggs develop without sperm (asexual)
Haplodiploidy sex determination

Wasps

Haploid male
Diagnosis of disease  Ch4
Fetal Chromosomal Analysis

Amniocentesis > week 14
needle into amniotic sac

Fluid contains fetal cells

Karyotype, DNA test

Risk of miscarriage = 1/300
Chorionic villus sample (CVS) ~week 8

Biopsy of chorion

More risky
Table 18-2 Number and Type of Chromosomal Abnormalities Among Spontaneous Abortions and Live Births in 100,000 Pregnancies
An Introduction to Genetic Analysis. 7th edition.
<table>
<thead>
<tr>
<th>100,000 PREGNANCIES</th>
<th>15,000 spontaneous abortions 7,500 chromosomally abnormal</th>
<th>85,000 live births 550 chromosomally abnormal</th>
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</thead>
<tbody>
<tr>
<td><strong>Trisomy</strong></td>
<td></td>
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</tr>
<tr>
<td>1</td>
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<td>0</td>
</tr>
<tr>
<td>2</td>
<td>159</td>
<td>0</td>
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<tr>
<td>3</td>
<td>53</td>
<td>0</td>
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<tr>
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<td>5</td>
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<td>6–12</td>
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<tr>
<td>21</td>
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<td><strong>Sex chromosomes</strong></td>
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<td>XYY</td>
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<tr>
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<td>4</td>
<td>44</td>
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<tr>
<td>XO</td>
<td>1350</td>
<td>8</td>
</tr>
</tbody>
</table>
Ch. 16 Variations in chromosomes

- Chromosomal aberration
  - Spontaneous
  - Induced

Visible aberration in 6/1000 live births
Deletions (del)

- Part of chromosome missing
- Observe large ones by karyotype
- If centromere lost $\rightarrow$ chromosome lost
- Cause
  - Chemicals, radiation
  - Unequal crossing over during meiosis
- If deletion homozygous $\rightarrow$ lethal
46,XX,del(7)(q21.12,q21.2)

Heterozygous del $\rightarrow$ pseudodominance
Cri du Chat

- 46, XY, 5p-  
  Microcephaly, myotonia, “cry of cat”, brain impairment

If individuals make it past childhood, symptoms lessen.
Duplications

- segment of a chromosome doubles
- May be tandem or reverse
- problems during meiosis
dup(5)(qter->q33.1::p15.3->qter)

- Sample of cord blood from stillborn male with anencephaly
Inversions (inv)

- 180° turnaround of segment
  - no loss of genetic material
  - may change length ratio of p/q arms

- Position effect
  - change in gene position with respect to centromere may influence expression
- Chromosome 5
- Human
- Chimp
Inversion may lead to abnormal cell growth
Translocations

- segment moves to other chromosome - interstitial or reciprocal exchange
- Individual has all genetic material, but what about gametes?
t(11;13) (q21;q14.3)

- parent who has translocation is phenotypically normal

- The gametes are not → multiple miscarriages
Translocation (cont.)

- Robertsonian fusion
  - ends of 2 acro- or telocentric break/fuse
  - 45 chromosomes but no, or little, loss of genetic material
Aneuploidy: chromosome # changes

- Nullisomy
  - Loss of homologous pair of chromosomes
  - Not viable in animals
Monosomy (only 1 viable in humans!)

- 45 XO
  - Turner Syndrome (1/2000 live births)

- Partial monosomy 46, 5p-
- Trisomy
- 47, 21+

(1/800 live births)

21 may be small, but contains 33,546,361 bp of DNA!
Down Syndrome = trisomy 21

- Developmental delays
- Possible heart defects, hearing loss, hypotonia, thyroid problems, obesity
- Epicanthic eye folds
- Wide tongues
- Greater risk of Alzheimer’s
Trisomy 13 (Patau)

- Fatal < 1 year (usually)
- Deaf, blind, cyclopia, polydactyly, cleft palate
- 1/5000 live births

47, XY, 13+
47, XY, 18+ (Edward’s)

- < few months (a few have lived 15 years)
- Clenched hands
- Crossed legs (preferred position)
- Feet with a rounded bottom (rocker-bottom feet)
- **Low birth weight**
- Low-set ears
- Mental deficiency
- Small head
- Small jaw
- Underdeveloped fingernails
- Unusual shaped chest

syndactyly
Normal chromosome complement

Diploid (2N)

Aneuploidy

Nullisomic (2N−2)

Monosomic (2N−1)

Doubly monosomic (2N−1−1)

Trisomic (2N+1)

Tetrasomic (2N+2)

Doubly tetrasomic (2N+2+2)

HUMAN NUMBER

46
Polyploidy = extra SETS of chromosomes
- Many plants are polyploid
- Some bees and wasps are monoploid
Somatic mosaics/chromosomes

More than one genetically distinct population of cells in individual

Ex: 46XX embryo, one cell loses an X due to non-disjunction

---→ 46,XX/45X mosaic

- Symptoms less severe than the standard Turners syndrome
Somatic mosaic single gene

- asymmetrical skin pigmentation in McCune Albright syndrome
- mutation in the GNAS1 gene occurs postzygotically in a somatic cell.
- All cells descended from mutated cell manifest features of McCune-Albright syndrome or fibrous dysplasia.
- Variable expressivity
Geep = mosaic combination of goat and sheep embryo

Courtesy of Dr. Gary Anderson, University of California at Davis
http://www.genome.gov/20519690

Genetic testing, sickle cell and heart disease
National Human Genome Research Institute
Barbara Beisecker, genetic counselor