Chromosomes

We can observe mitotic chromosomes using light microscopy

Chromosomes condense during mitosis
(that's why we can see them with the microscope)

Smallest human chromosome
1.4 cm long stretched out
2 microns in mitosis
Compacted 7000 fold

Amniocentesis
Why amniocentesis and karyotyping?

Meiosis usually results in gametes with a single set of chromosomes!

Nondisjunction in meiosis I or II results in gametes with an extra or missing chromosome. When these gametes fuse, the fusion results in zygotes with an extra or missing chromosome, a situation termed aneuploidy!

What are the consequences of aneuploidy in humans?
Autosomes first!

All monosomic (43 autosomes; missing an autosome) spontaneously abort.

Almost all trisomic (45 autosomes; an extra autosome) fetuses spontaneously abort! There are three exceptions.

Trisomy 13; Patau Syndrome
Trisomy 18; Edwards Syndrome

Most fetuses spontaneously abort. Those that make it die in first year.

Trisomy 21; Down Syndrome

Can survive to age 50
Mental retardation

But, why do aneuploid fetuses die?

1000s of genes are over or under expressed!

Turner syndrome, XO

Female
Short, wide-chested
Rudimentary ovaries
Sterile
Normal intelligence

But the rules are different for the sex chromosomes!
ALL autosomal monosomics die, BUT XO individuals survive and are relatively normal!!!

Klinefelter syndrome, XXY

- Male
- Phenotype of syndrome not apparent until puberty
- Breast development
- Low fertility
- Subnormal intelligence

Karyotype: 47,XXXXY

XYY Syndrome

XXX Females are normal

XXX and XXXXX females also exist

AHA!! Yet another difference between sex chromosomes and autosomes.

Autosomal trisomies die, but XXY, XYY, XXX, and XXXX can survive.

Two conclusions

Y associated with maleness

Abnormal # sex chromosomes tolerated
Why do individuals lacking an autosome or having an extra autosome die?

1000s of genes under or over expressed!!

OK, but then why do XO, XXX, XXXX and XXXXX individuals survive?

X inactivation/dosage compensation

In mammalian females, early in embryonic development each cell inactivates one X chromosome.

Males have one X chromosome and females have two.

XXX, XXXX and XXXXX individuals survive because only one X chromosome is expressed!

Barr bodies are inactivated X chromosomes

<table>
<thead>
<tr>
<th>Karyotype</th>
<th># Barr bodies</th>
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<tbody>
<tr>
<td>XY</td>
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XXX, XXXX and XXXXX individuals survive because only one X chromosome is expressed!
Whoa!!! All mammalian females are mosaic!!!

These cells express only paternal X chromosome genes.

These cells express only maternal X chromosome genes.

X inactivation results in black and orange patches on Calico cats.

Female Calico cats have black and orange alleles of an X-linked gene.

Other consequences of X inactivation

X-linked genetic diseases can be mosaic in females

The Y chromosome is necessary and sufficient for male development!

Three generations of females heterozygous for X linked anhidrotic ectodermal dysplasia (absence of sweat glands). Areas without sweat glands are shown in green.