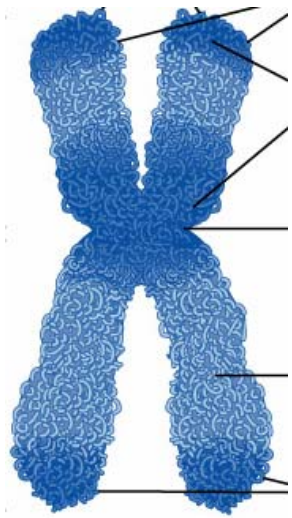
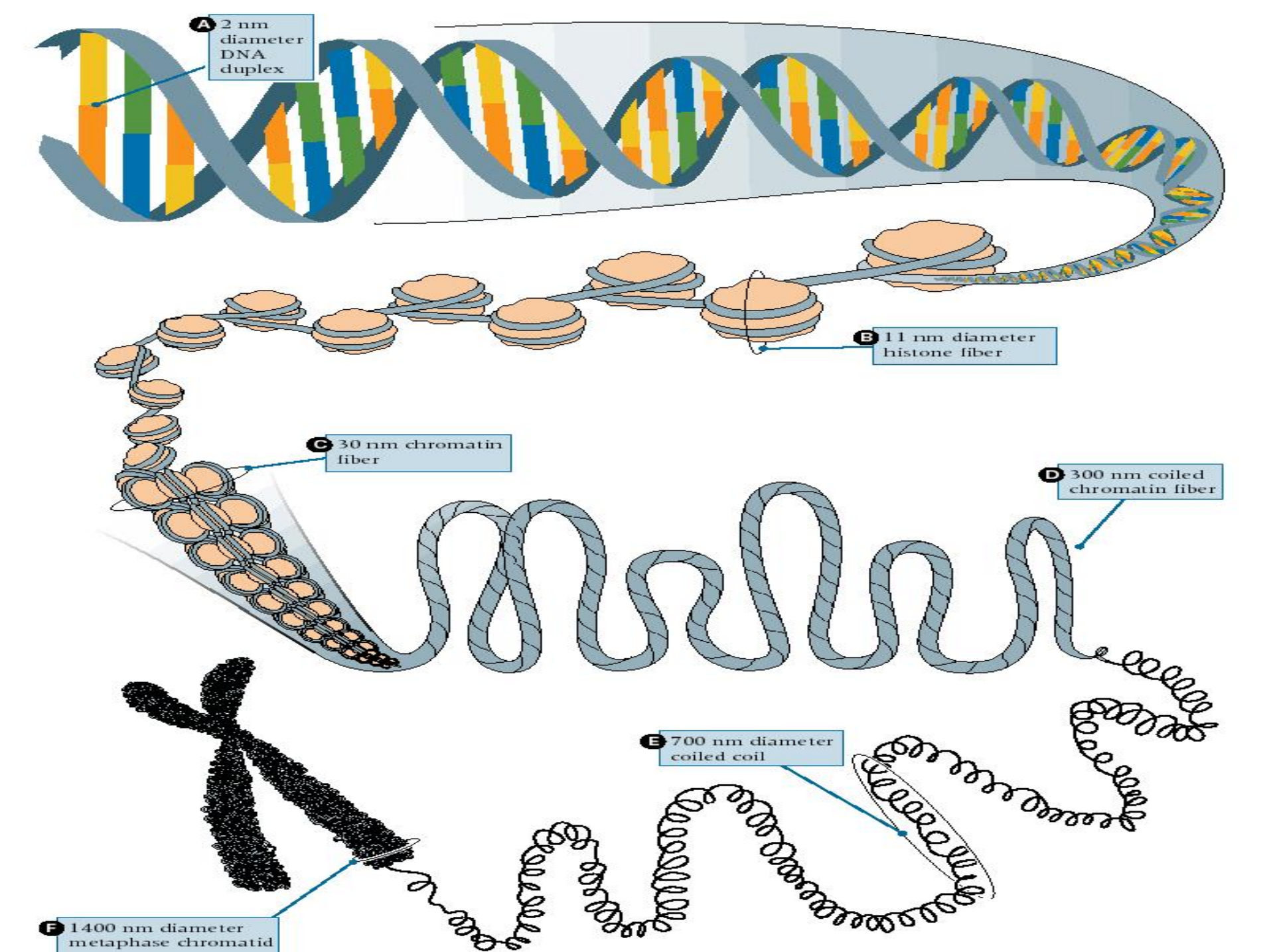
Chromosomes

Chapter 13

What is a Chromosome?

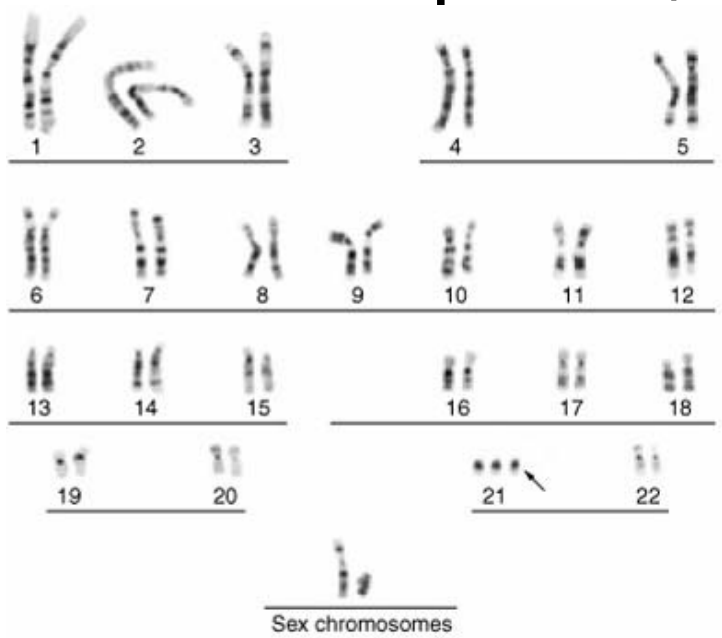
- Chromosome is the highly condensed form of DNA
- Wrapped into nucleosomes
- Wrapped into chromatin fiber
- Condensed during metaphase into the familiar shape
- Humans have 22 autosomal pairs
- And one pair of sex chromosomes




A 2 nm diameter DNA duplex
B 11 nm diameter histone fiber
C 30 nm chromatin fiber
D 300 nm coiled chromatin fiber
E 700 nm diameter coiled coil
F 1400 nm diameter metaphase chromatid

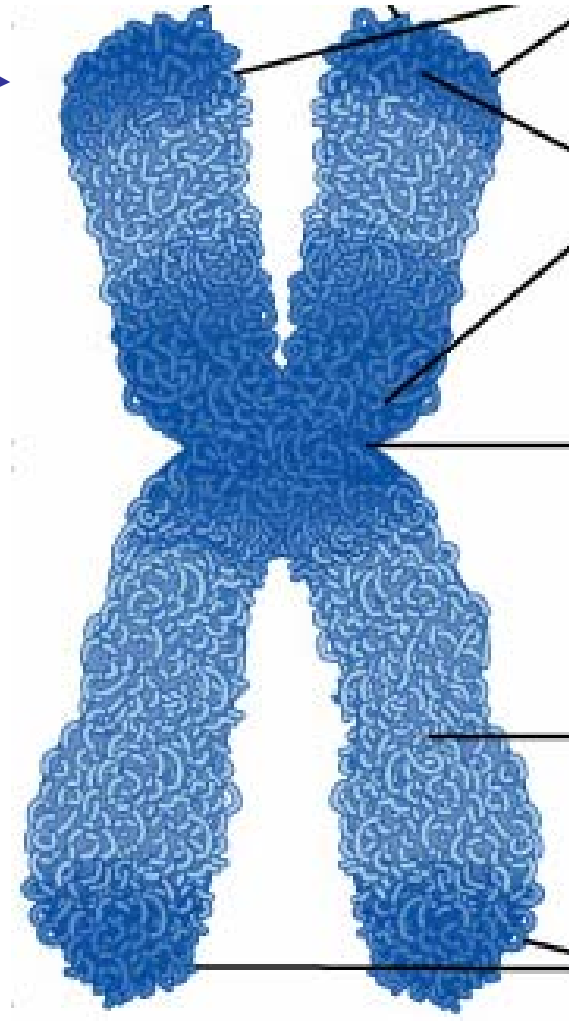
Cytogenetics

- Study of chromosomes and chromosomal abnormalities
- Study Karyotypes – picture of an individual's chromosomes in Metaphase, spread out on a slide



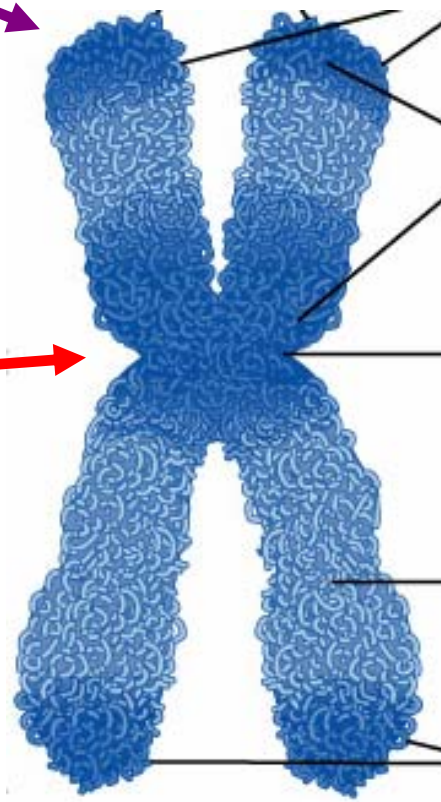
Chromosome Parts:

- Heterochromatin:
  - More condensed
  - Silenced genes (methylated)
  - Gene poor (high AT content)
  - Stains darker
- Euchromatin:
  - Less condensed
  - Gene expressing
  - Gene rich (higher GC content)
  - Stains lighter



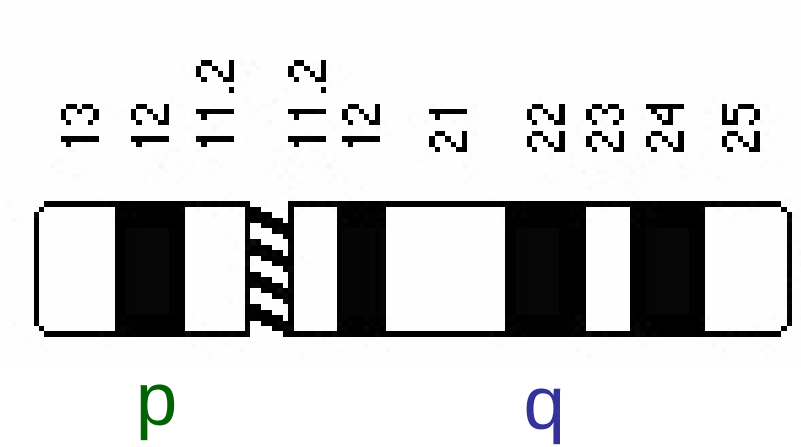
Chromosome Parts:

- Telomeres – chromosome tips
  - Repeats
  - Act as sort of biological clock
  - Being whittled down at each Mitosis
- Centromeres – middle
  - Highly condensed
  - Also repetitive sequence
  - Region where spindle fibers attach
  - Pulling chromatids apart during Mitosis



Chromosome Parts:

- p arm – the smaller of the two arms
  - p stands for petite
- q arm – the longer of the two arms
- Bands are numbered from centromere outward



Chromosome Types

There are four types of chromosomes:

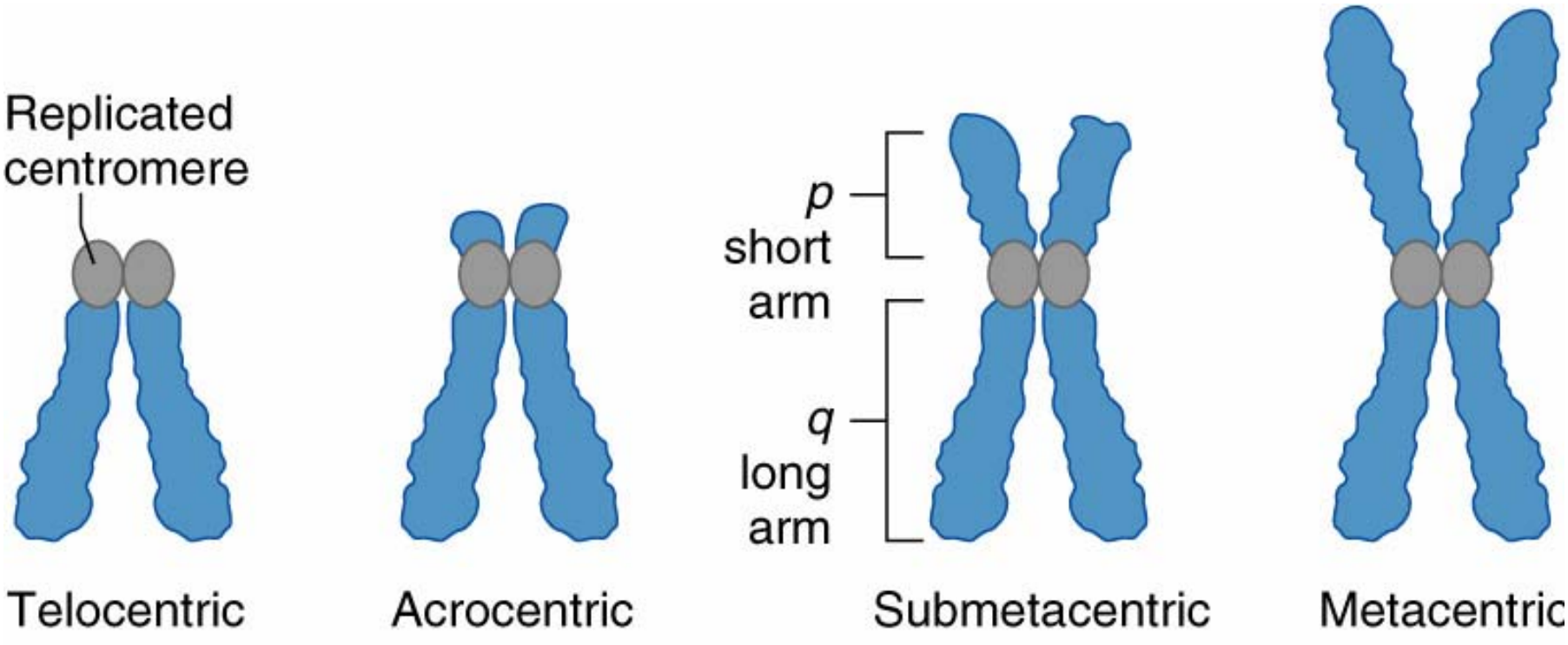
1. Telocentric
2. Acrocentric
3. Submetacentric
4. Metacentric

- Divided based on the position of the centromere

Chromosome Types:

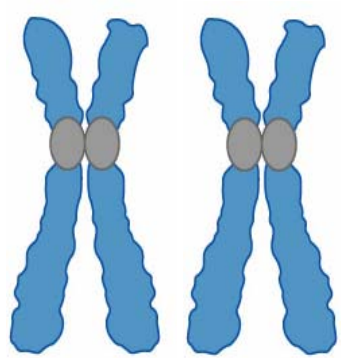
1. Telocentric – no p arm; centromere is on end
2. Acrocentric – very small p arm; centromere is very near end
3. Submetacentric – p arm just a little smaller than q arm; centromere in middle
4. Metacentric – p and q arms are exactly the same length; centromere in exact middle of chromosome

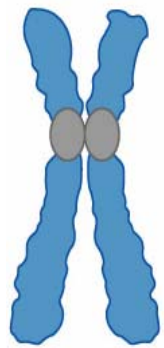
Chromosome Types:



Things to remember…

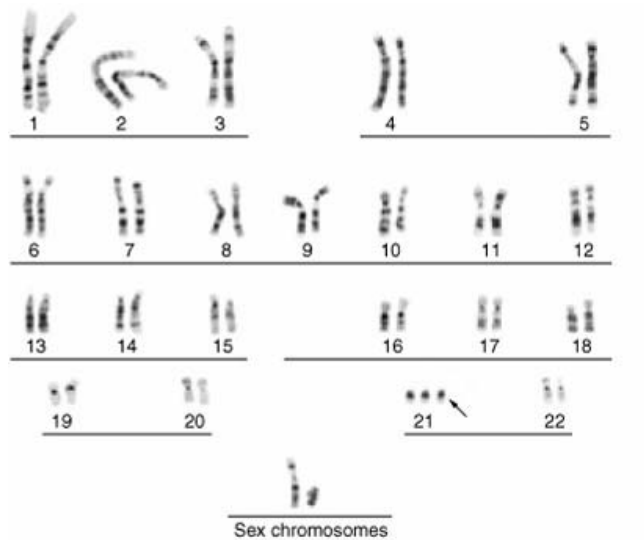
- Homologous chromosomes are not identical
  - Can have different alleles of genes
- Sister chromatids are identical
  - Form as cells go through S phase (replication)
  - Attached to each other by centromere
  - Until Anaphase of Mitosis
  - Once separated each is again referred to as a chromosome





Karyotypes

- Individual's chromosomes in Metaphase, spread out on a slide
- Used to study chromosomes
- Identify chromosomal abnormalities
- Cytogenetics



Making a Karyotype:

1. Obtain any cells with nucleus from patient under study
   - Any cell other than red blood cells
2. Arrest and isolate cells in mitosis
   - Metaphase of mitosis
3. Spread out chromosomes
4. Identify each chromosome from each other
   - Some sort of staining procedure

Making a Karyotype:

1. Arrest the cells in Metaphase
    1. Chemical Colchicine used
2. Spread out chromosomes
    1. Use osmosis to swell the cells
    2. Squash the swollen cells under a slide
3. Identifying chromosomes
    1. G-staining – stains heterochromatin vs. euchromatin

Making a Karyotype:

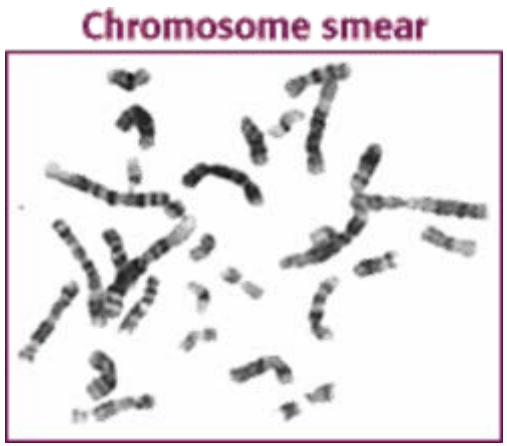
Identifying chromosomes

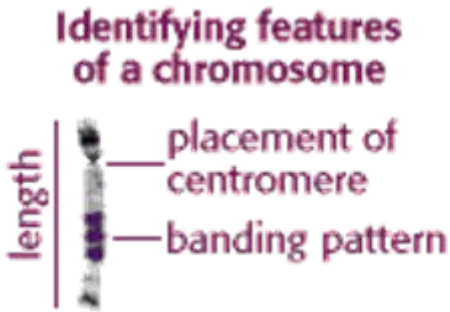
1. G-staining:
   - Stains heterochromatin vs. euchromatin
   - Light and dark banding pattern
2. FISH – Fluorescence In Situ Hybridization
   - “Paint” chromosomes
   - Each a different color
3. Labeled DNA Probes
   - Use a small piece of DNA that will bind to it’s complementary base pair

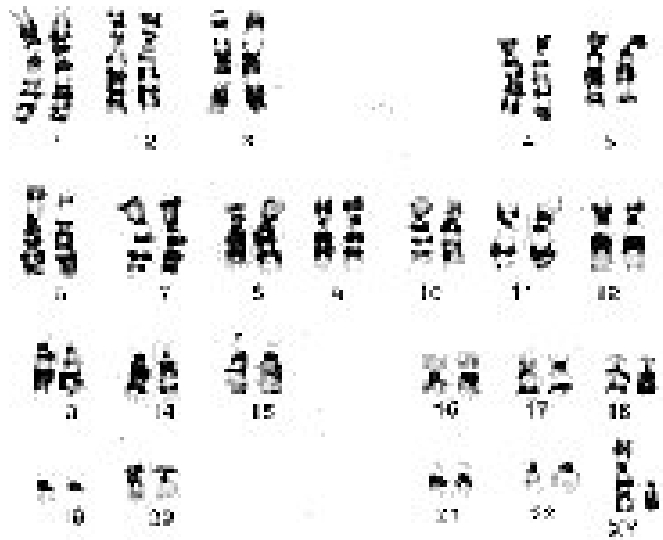
Examining Karyotypes

- Identifying the wrong number of chromosomes is easy
- Finding large deletions, duplications or rearrangements is possible with G-banding staining
- Finding smaller deletions, duplications or rearrangements or identifying individuals genes requires FISH or DNA probe

Karyotype







Go to this site to learn how to create a virtual karyotype with real patient samples:
http://www.biology.arizona.edu/human_bio/activities/karyotyping/karyotyping.html

What can we learn from Karyotypes?

- Can see chromosomal abnormalities:
  - An extra chromosome
  - A deleted chromosome
  - Large deletion
  - Large duplication
  - Rearranged chromosome parts
  - Abnormal structure

Abnormal Number:

Polyploidy:

- Complete extra set of chromosomes
  - Three of every chromosome
  - Cannot survive to birth

Aneuploidy:

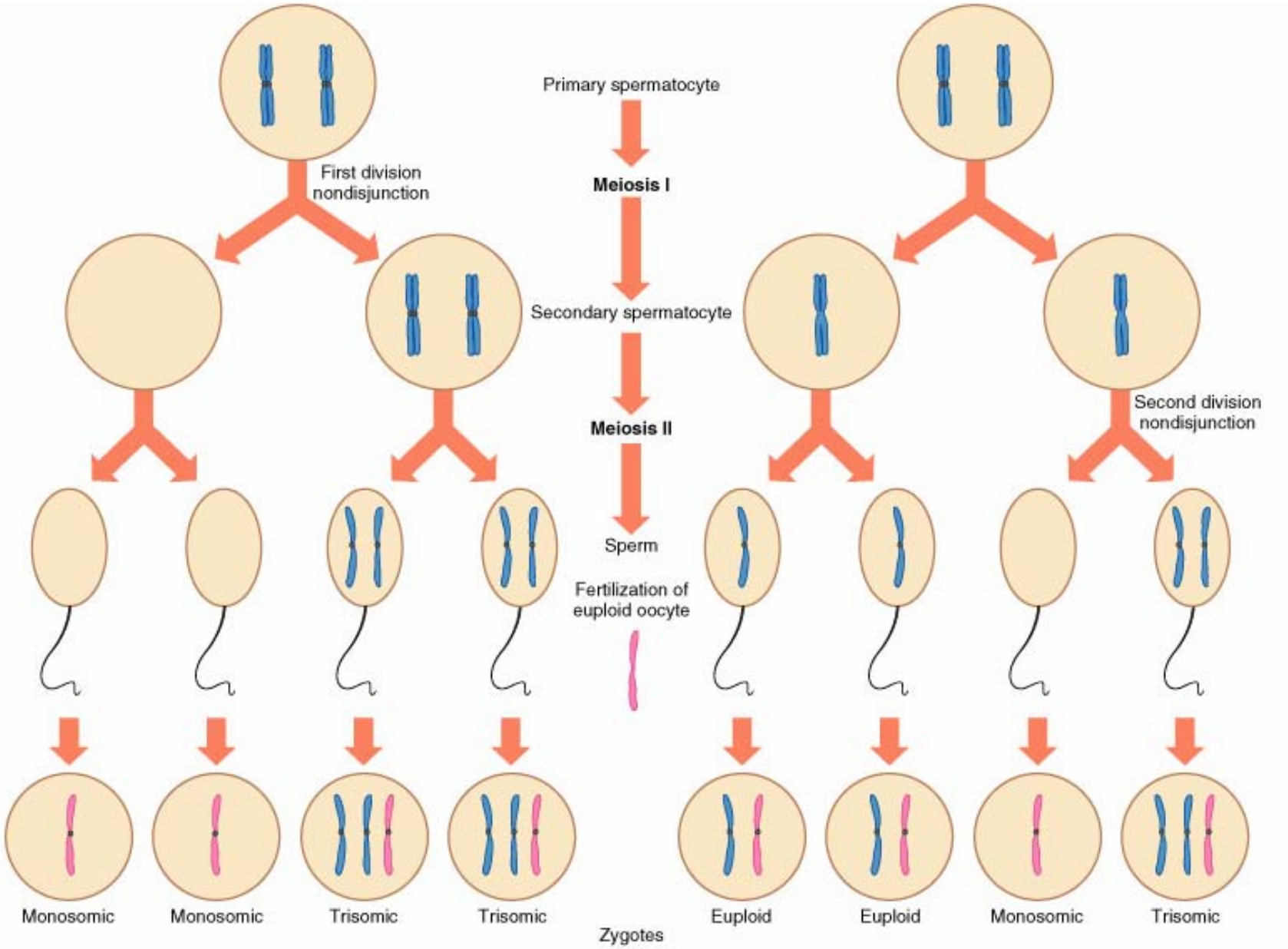
- Missing or extra of one chromosome
  - Monosomy – missing one chromosome
  - Trisomy – one extra chromosome
  - Only Trisomy 13, 18 and 21 are viable

Non-disjunction

Unequal division of chromosomes during Meiosis

- Can happen to either sperm or oocyte
- Form one gamete with two copies of same chromosome
- Other gamete with zero copies of that chromosome
- Different outcomes if happens at first or second stage of Meiosis

Non-disjunction



Why are only some Aneuploidies viable?

- Why only Trisomy 13, 18 and 21 for autosomes?
- Why can sex chromosomes be monsomic or trisomic?

Deletion or Duplication

Deletion:

- Large part of one chromosome has been lost during mitosis
- Vary in size – larger is more severe

Duplication:

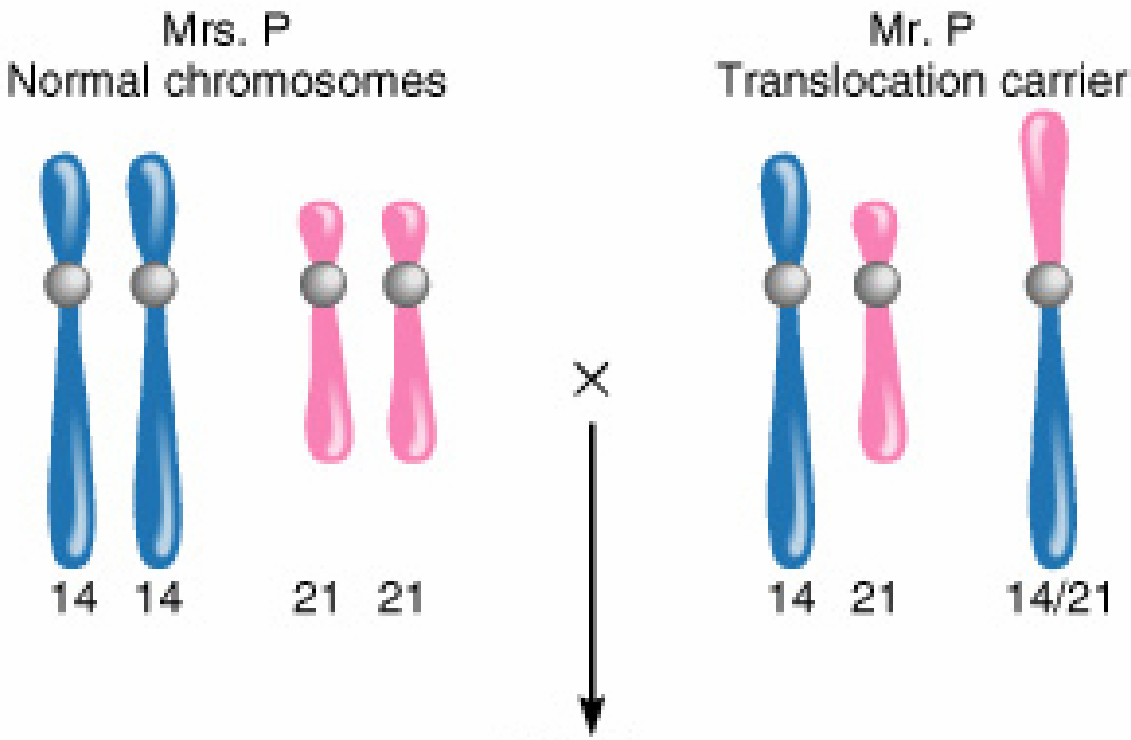
- Large part of one chromosome has been duplicated on same chromosome
- Vary in size – larger is more severe

Translocations

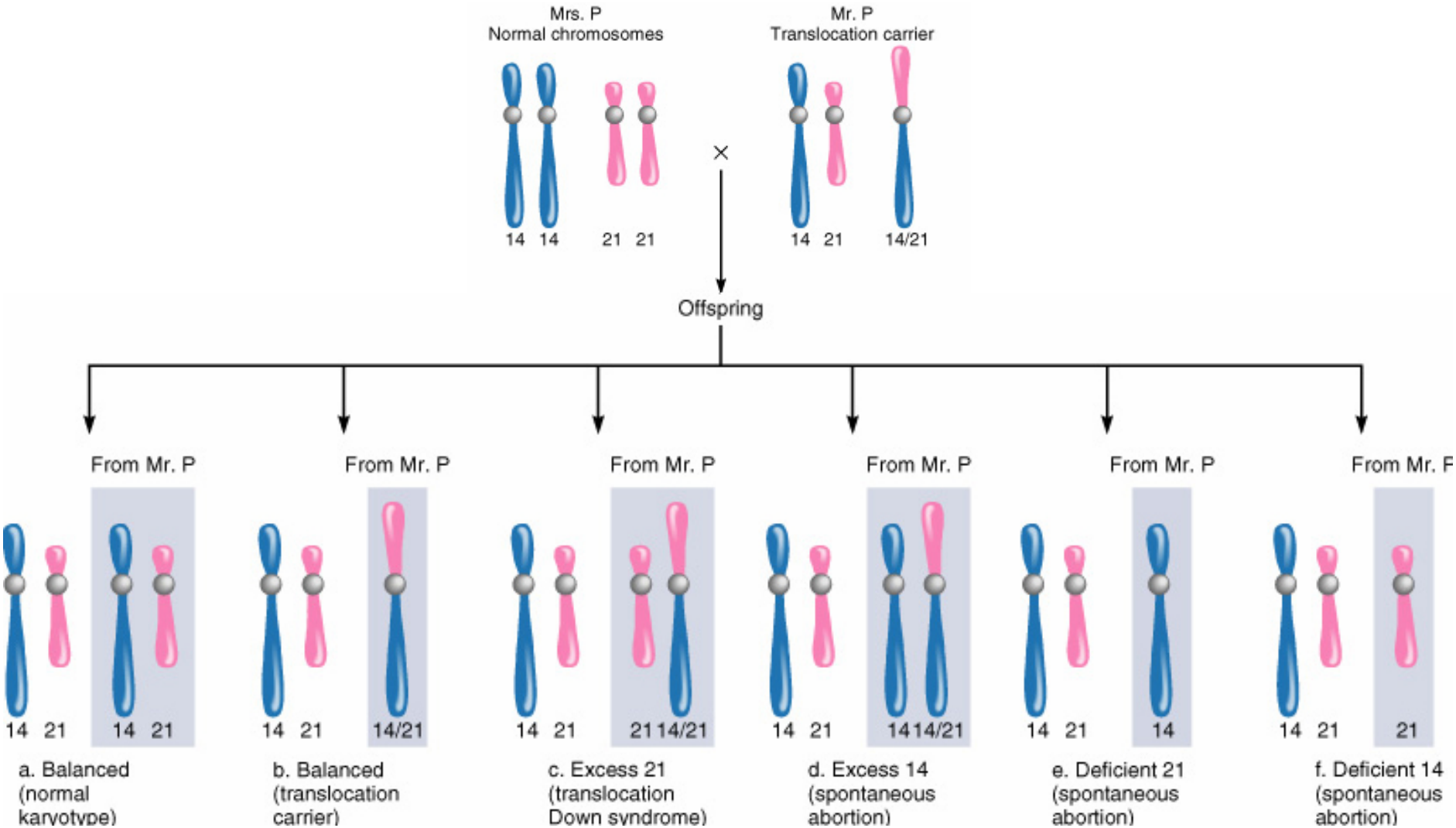
Non-homologous chromosomes have exchanged pieces (crossed over)

1. Robertsonian Translocation
   - Two q arms of two different chromosomes come together
   - Two p arms are lost entirely
2. Reciprocal Translocation
   - Two different chromosomes exchange parts
   - Since all parts are still present – often normal

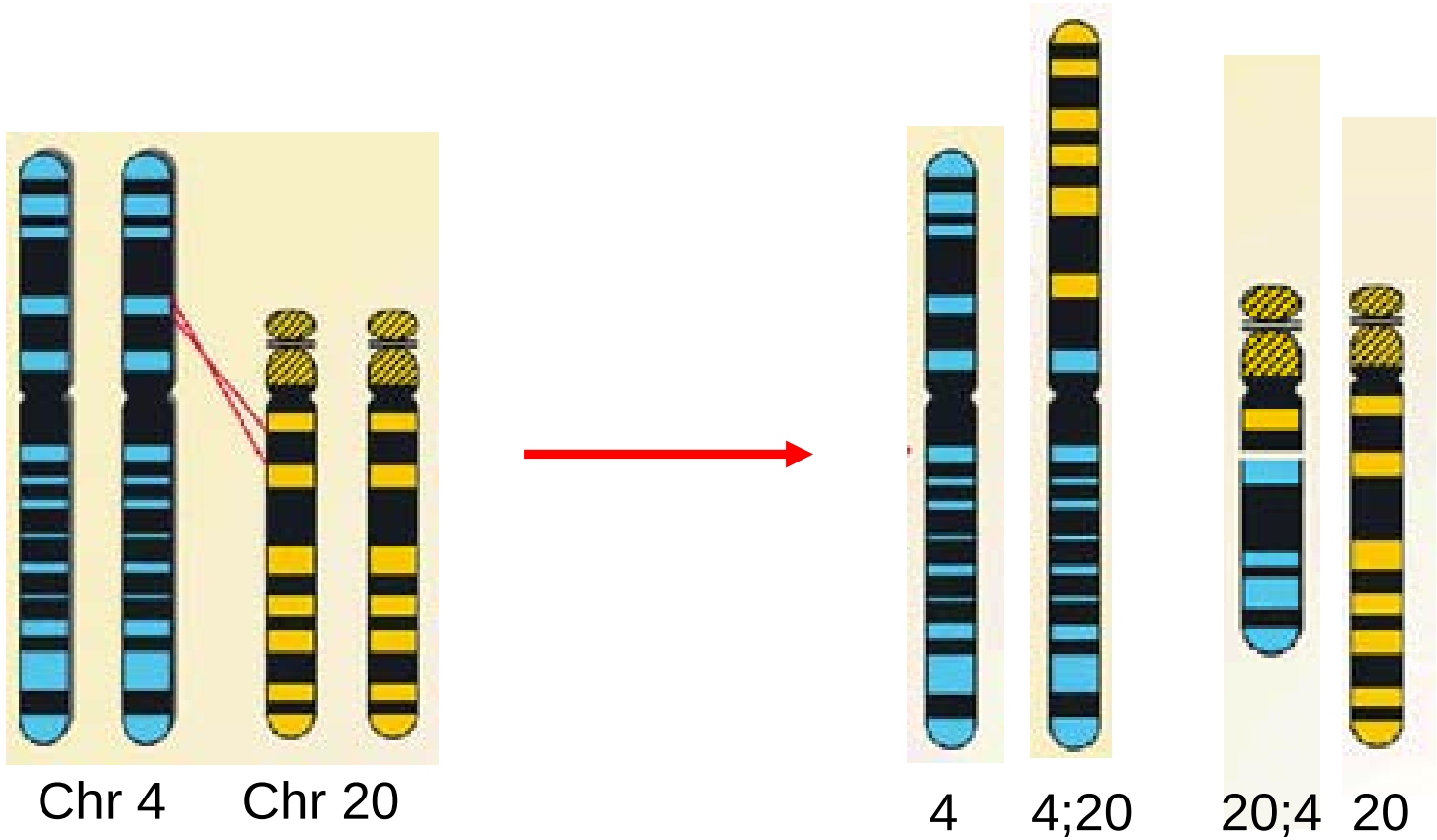
Robertsonian Translocation



Robertsonian Translocation



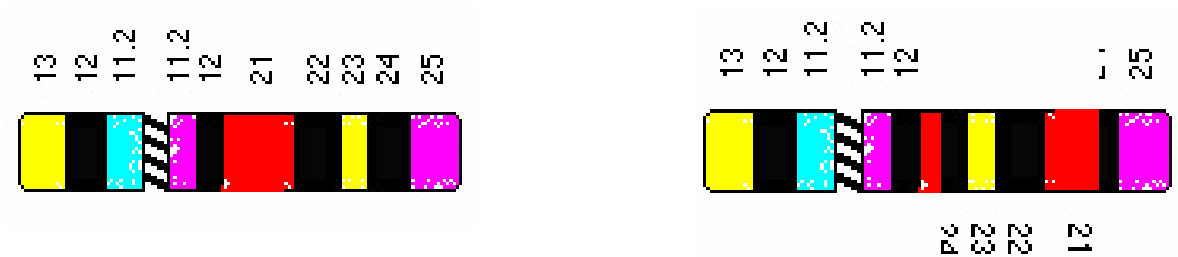
Reciprocal Translocation



- Individual is usually fine
- Unless translocation break point in middle of a gene
- Think about what happens when this person has children

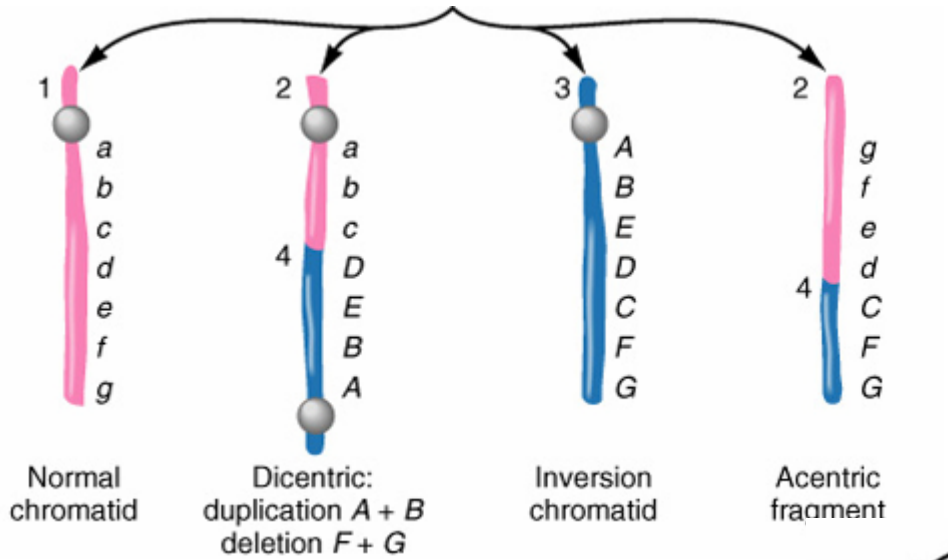
Inversions

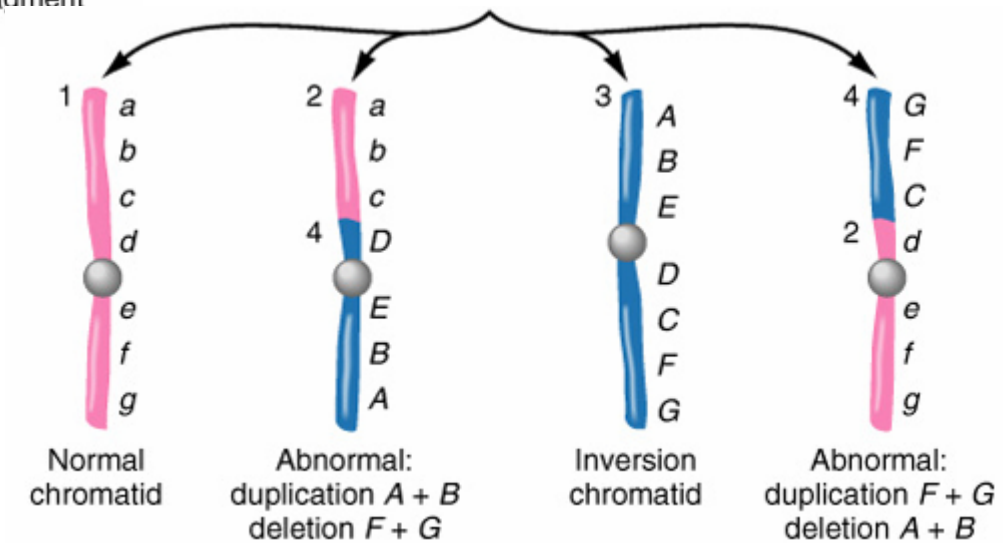
One part of chromosome has been flipped around in opposite direction



- Again, individual may be normal
- Unless inversion breakpoints are in middle of a gene
- Or unless inversion affects centromeres

Possible Inversions





Abnormal Structure

Isochromosomes:

- Have two identical arms
- Two p’s or two q’s and not the other

Ring chromosomes:

- Telomeres are lost, or don’t function
- So one end of chromosome attaches to other end forming a ring
- Cannot undergo mitosis successfully

Summary

Type of Abnormality	Definition
Polyploidy	Extra chromosome sets
Aneuploidy	An extra or missing chromosome
Monosomy	One chromosome absent
Trisomy	One chromosome extra
Deletion	Part of a chromosome missing
Duplication	Part of a chromosome present twice
Translocation	Two chromosomes join long arms or exchange parts
Inversion	Segment of chromosome reversed
Isochromosome	A chromosome with identical arms
Ring chromosome	A chromosome that forms a ring due to deletions in telomeres, which cause ends to adhere

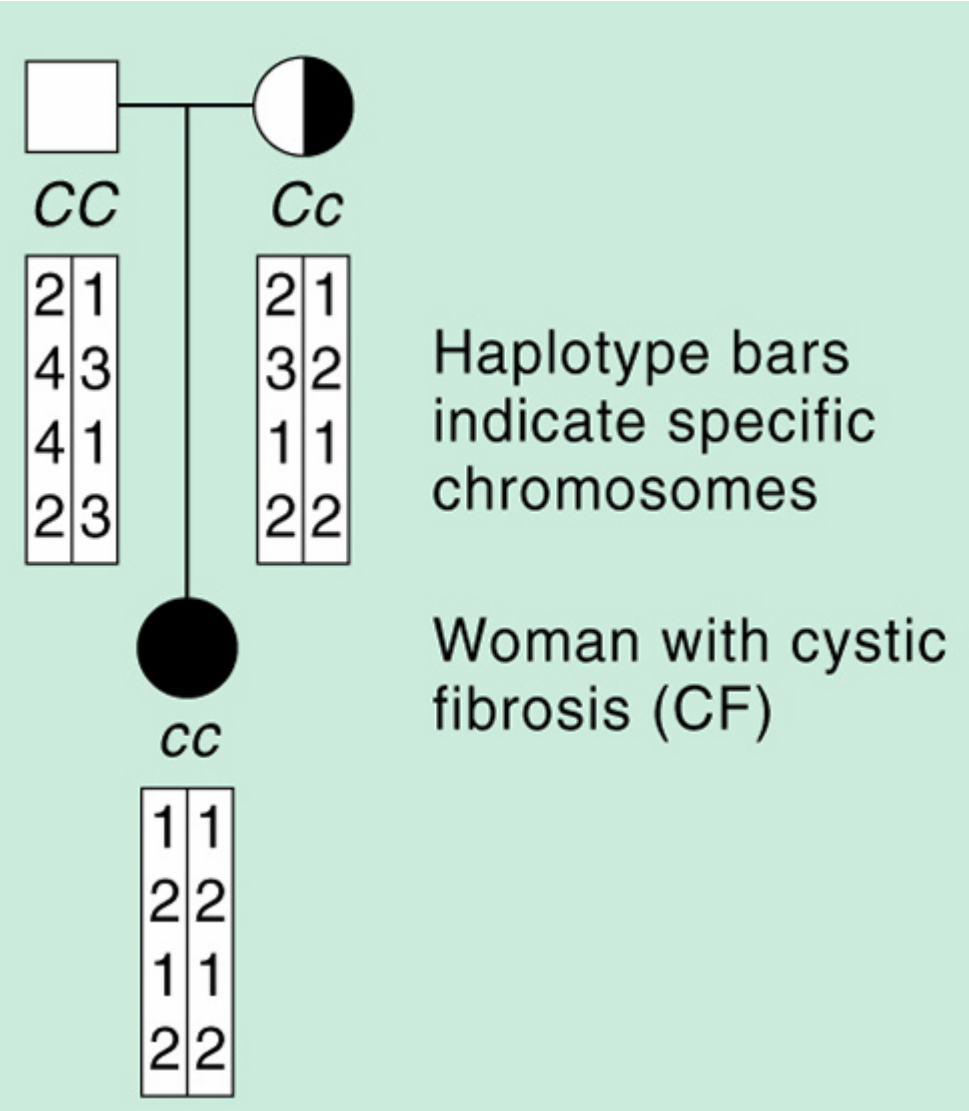
Uniparental Disomy

When nondisjunction occurs in both the mother and the father's gametes

Causing two copies of one chromosome to come only from one parent

- "Two bodies, one parent"
  - Bodies are chromosomes
- Incredibly rare event
- More often nondisjunction leads to either monosomy or trisomy

Uniparental Disomy



Which chromosome is duplicated?

What did father's sperm look like?

What did mother's oocyte look like?

Why does woman have CF?

Summary

- Know major parts of chromosome
- Know difference between sister chromatids and homologous chromosomes
- Know karyotypes:
  - How to make them
  - What can and can't interpret from them
  - FISH, G-banding, DNA probe
- Know types of chromosomal abnormalities
- Don't worry about diseases

Next Class:

- Homework – Chapter Thirteen Problems;
  - Review: 1, 3, 4, 9, 12
  - Applied: 1, 2, 4, 12
  - Also – write out at least 2 questions about material to review on Monday

- Review Chapters 9-13 and notes

Next Class:

Review Chapters 9-13

- Go through your review questions
- Exam 2 – October 25th