Chromosomes

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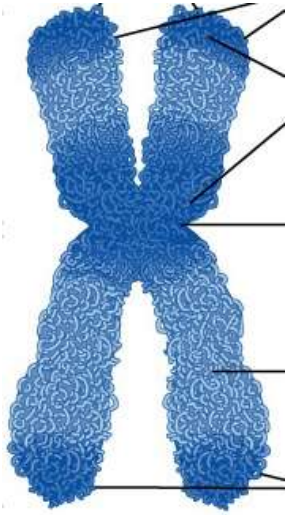
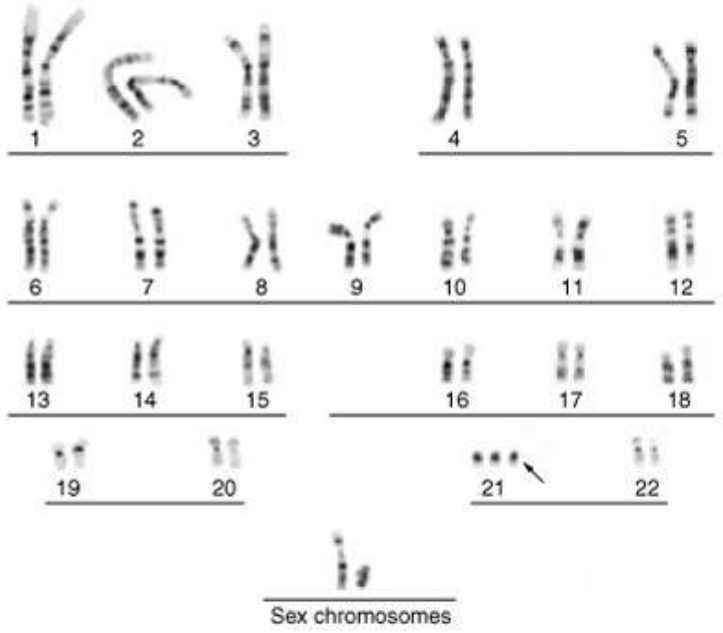
What is a Chromosome?

- 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



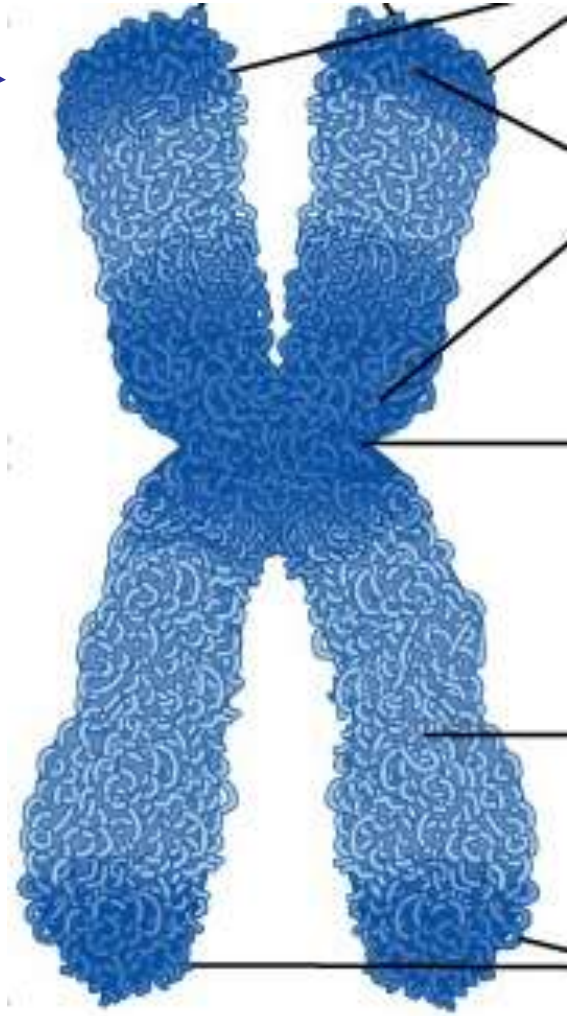
Cytogenetics

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



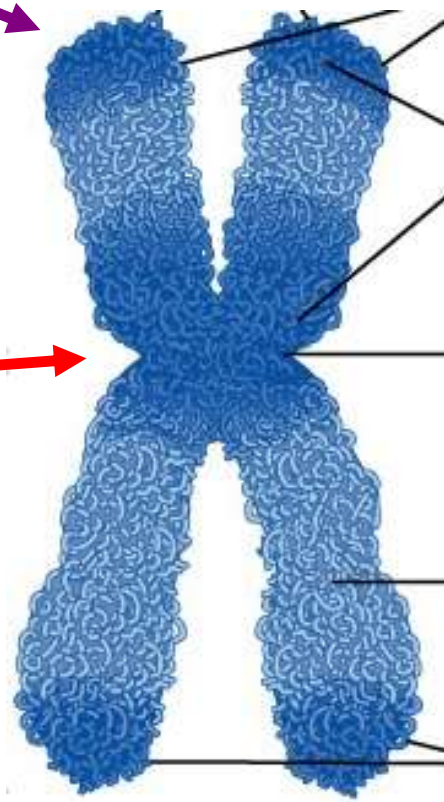
Chromosome Parts:

- 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



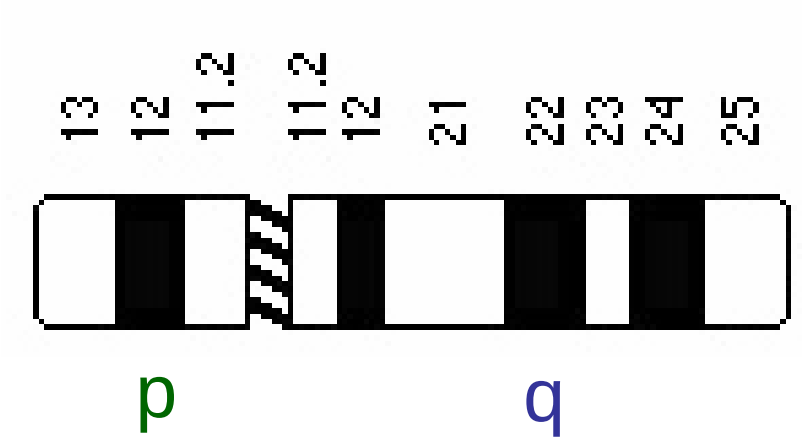
Chromosome Parts:

- 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:

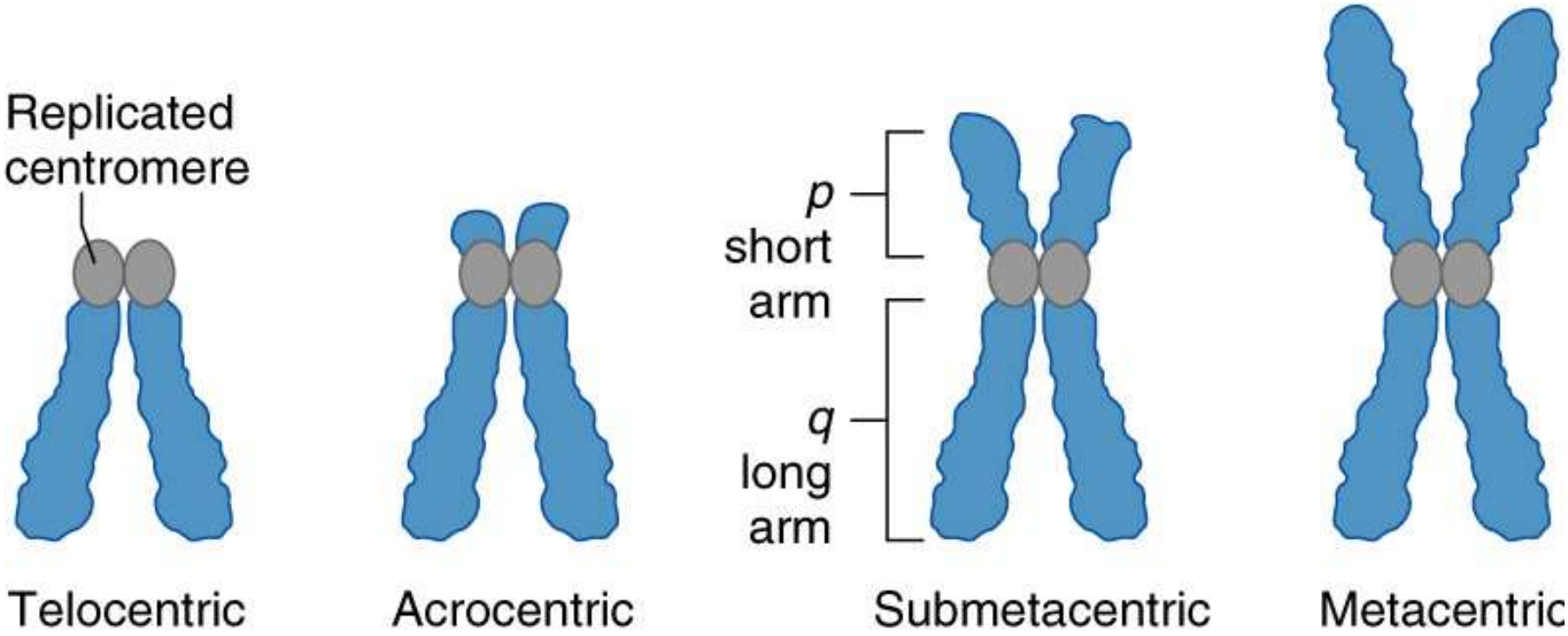
1. Telocentric
2. Acrocentric
3. Submetacentric
4. Metacentric

- Divided based on the position of the centromere

Chromosome Types:

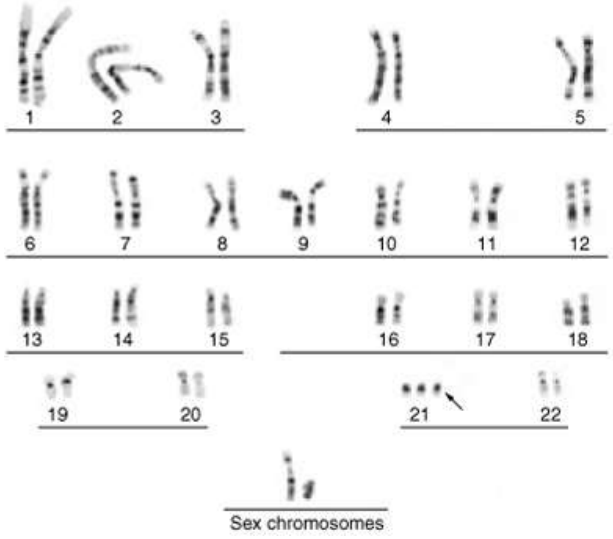
1. Telocentric – no p arm; centromere is on end
2. Acrocentric – very small p arm; centromere is very near end
3. Submetacentric – p arm just a little smaller than q arm; centromere in middle
4. Metacentric – p and q arms are exactly the same length; centromere in exact middle of chromosome

Chromosome Types:



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:

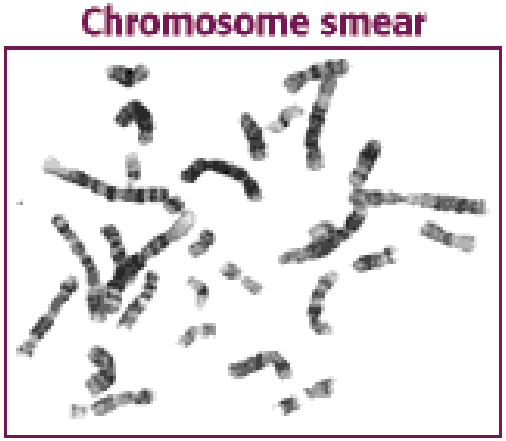
Identifying chromosomes

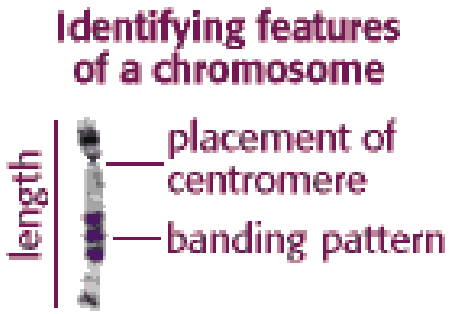
1. G-staining:
   - Stains heterochromatin vs. Euchromatin
   - Light and dark banding pattern
2. FISH – Fluorescence In Situ Hybridization
   - “Paint” chromosomes
   - Each a different color
3. Labeled DNA Probes
   - Use a small piece of DNA that will bind to it’s complementary base pair

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:

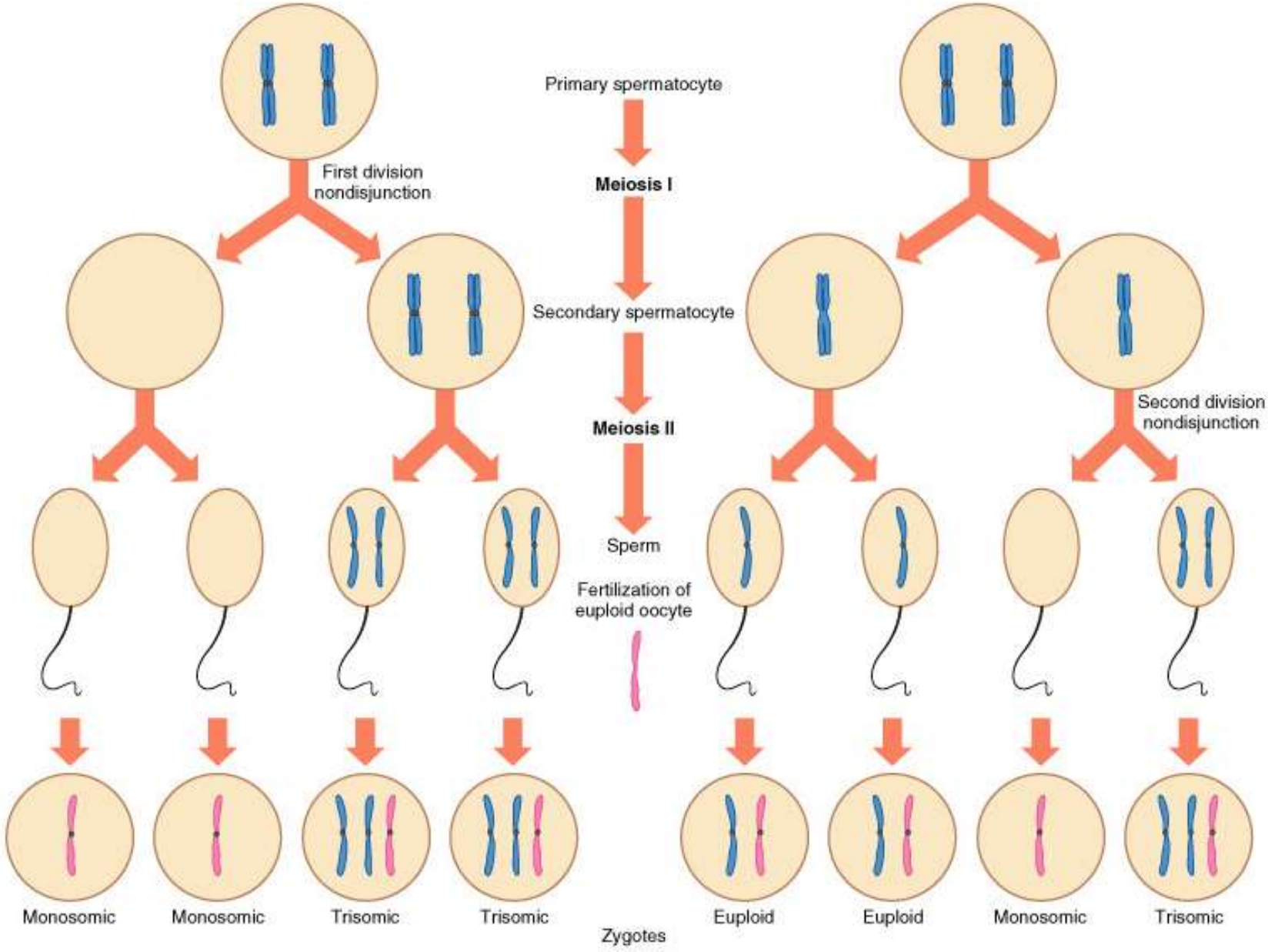
- Missing or extra of one chromosome
  - Monosomy – missing one chromosome
  - Trisomy – one extra chromosome
  - Only Trisomy 13, 18 and 21 are viable

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



Deletion or Duplication

Deletion:

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

Duplication:

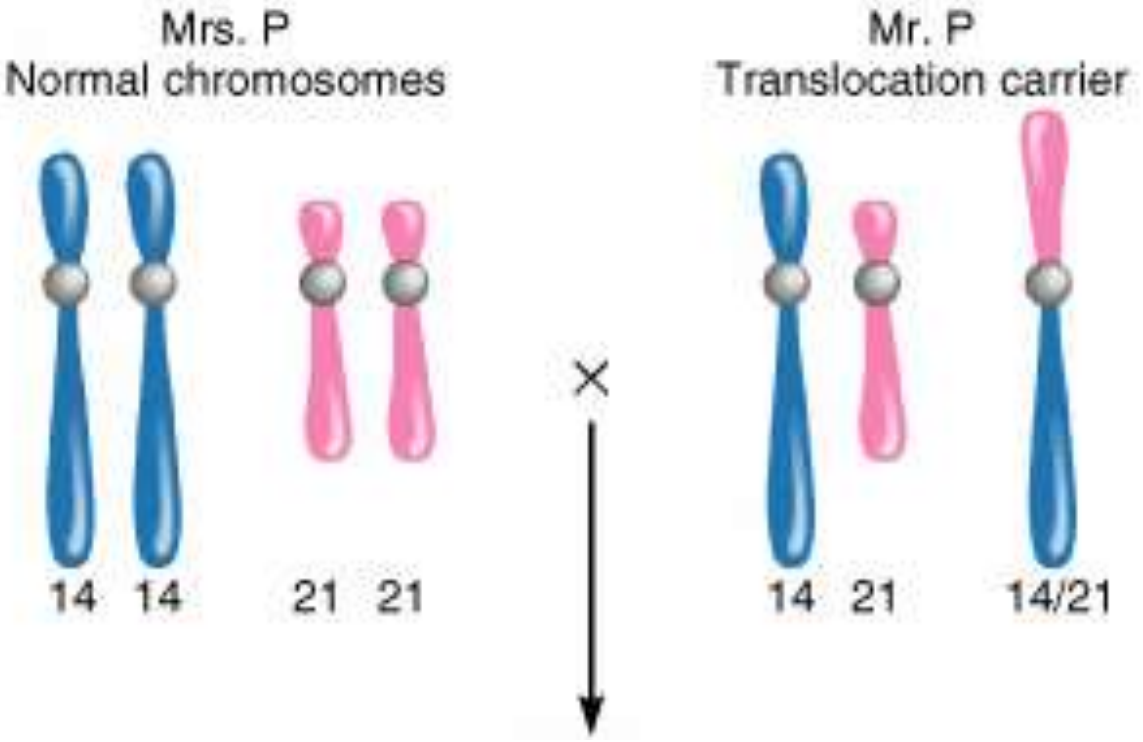
- Large part of one chromosome has been duplicated on same chromosome
- Vary in size – larger is more severe

Translocations

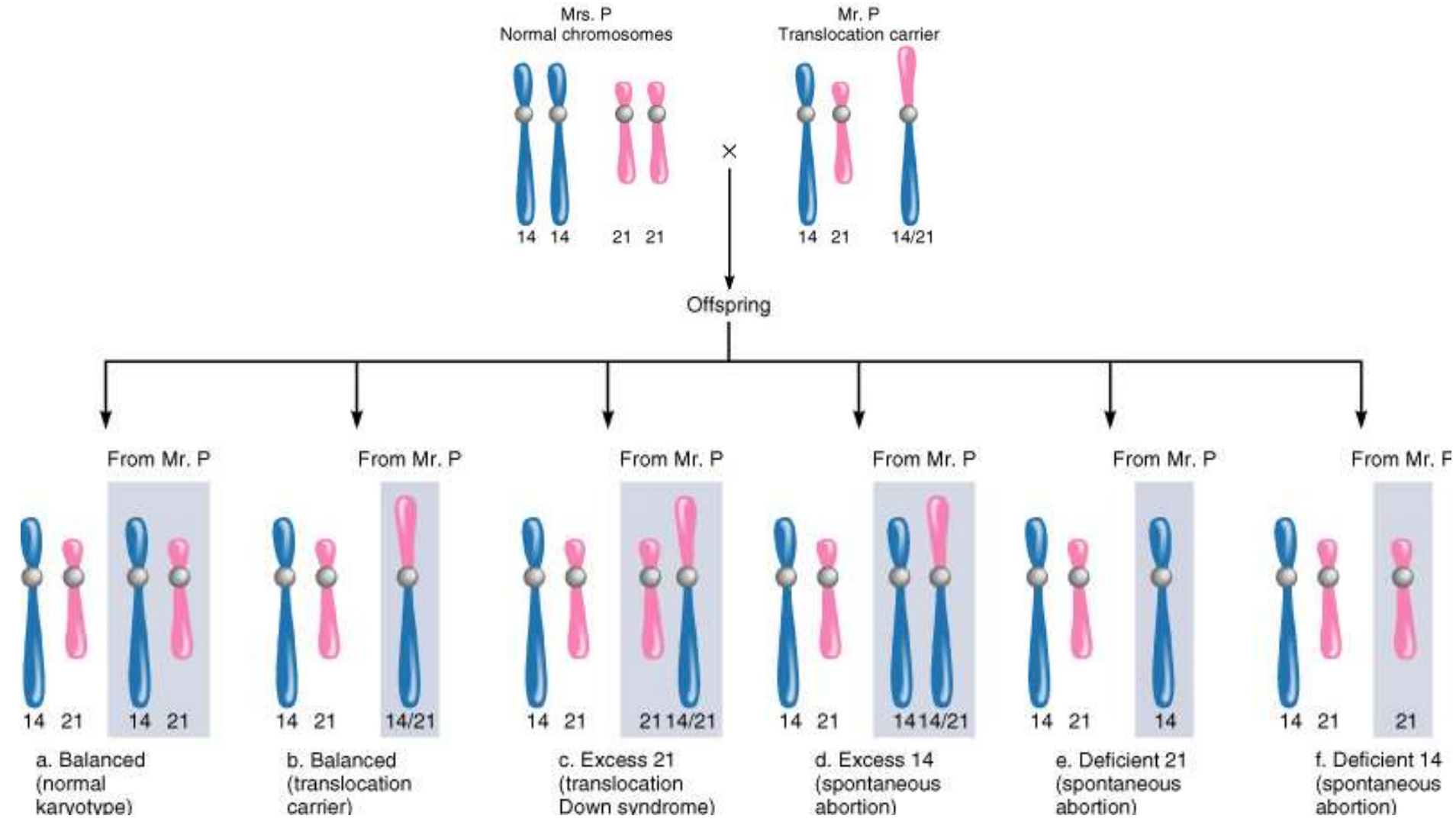
Non-homologous chromosomes have exchanged pieces (crossed over)

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

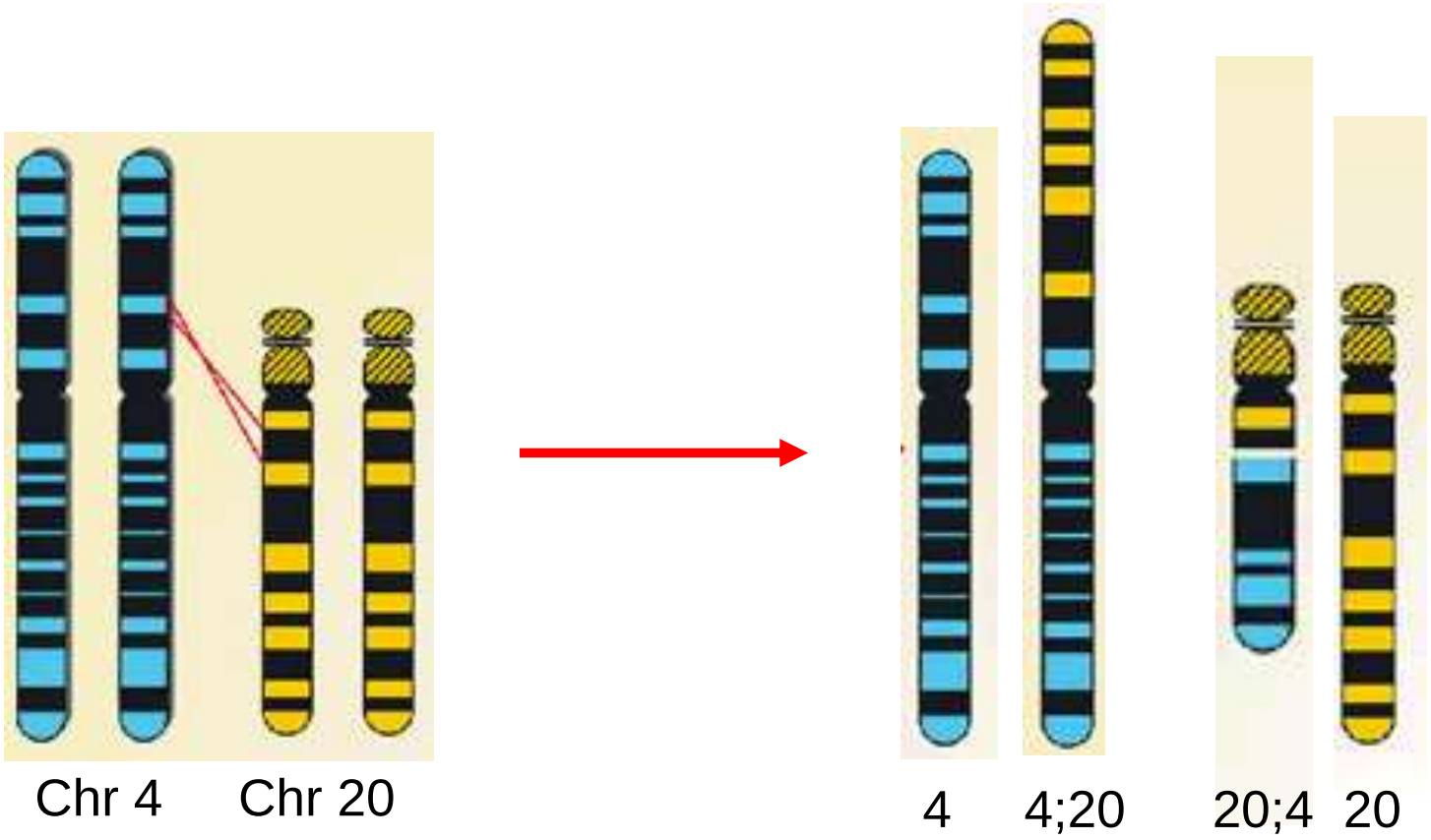
Robertsonian Translocation



Robertsonian Translocation



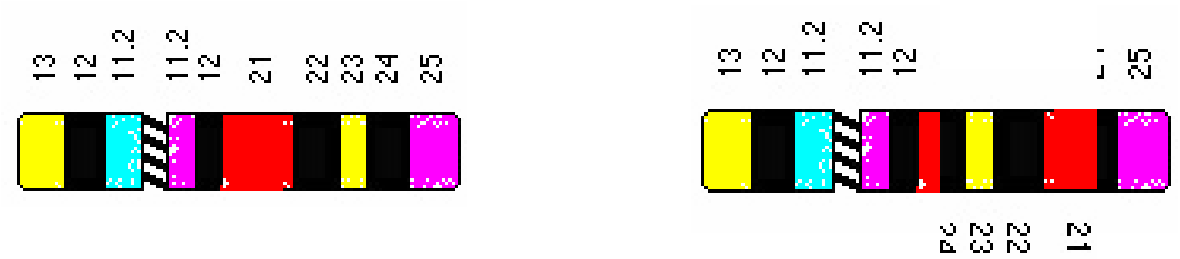
Reciprocal Translocation



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

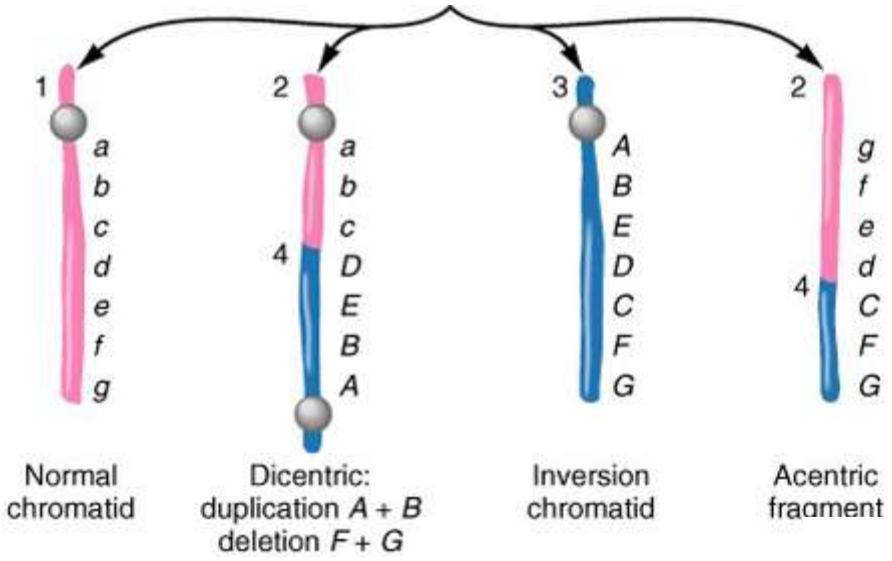
Inversions

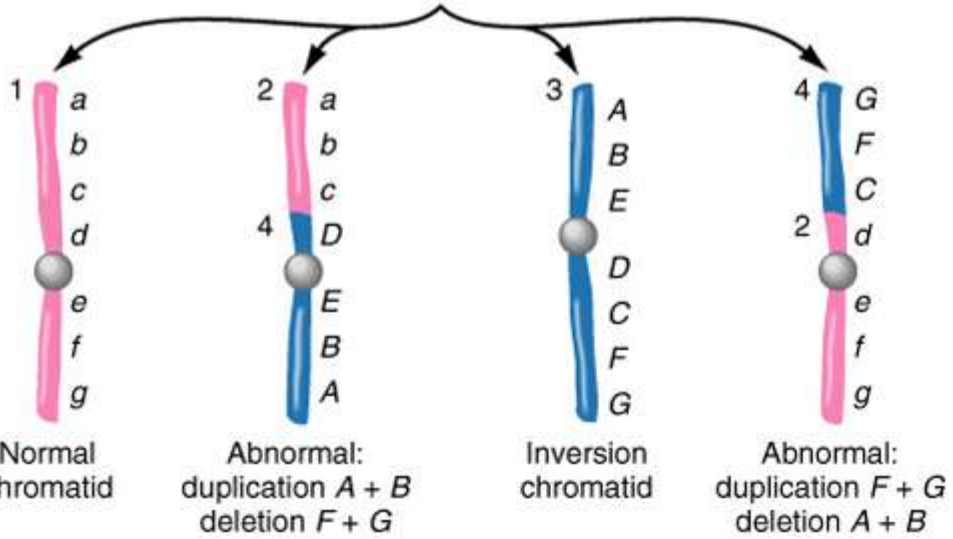
One part of chromosome has been flipped around in opposite direction



- 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