# Human Genetics

Human Chromosomes: Genotypes/Phenotypes

# Lecture objectives

**By the end of this lecture, the students should be able to:**

1-Describe the number, structure, and classification of human chromosomes.
2-Explain what a Karyotype is and how it is obtained.
3-Explain Genotype and Phenotype
4-Describe chromosomal banding and explain its use.
5-Describe the process of in situ hybridization and the information it provides

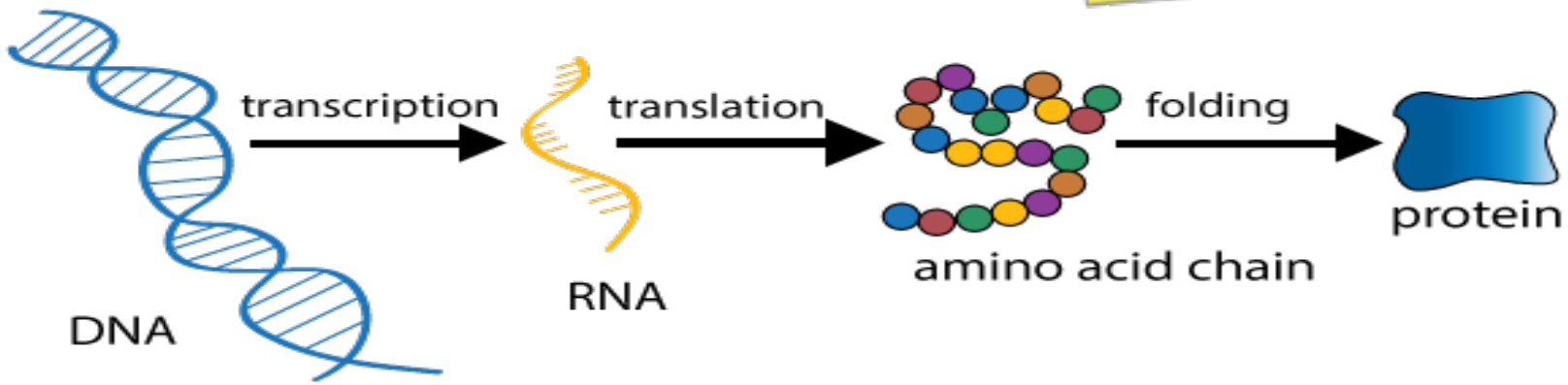
# Gene Expression

**Only the folded protein can perform function.**

**Note :** cell machinery copies the code making an mRNA molecule. (Transcription) This moves into the cytoplasm.

Ribosomes read the code and accurately join amino acids together to make a protein. (Translation)

**Nucleus in cell** → **Chromosome in nucleus** → **Gene in chromosome** → **Gene has DNA**




For further explanation:
https://m.youtube.com/watch?v=OEWOZS_JTgk

# Eukaryotic cells

* Eukaryotic cells present in humans and some other micro-organisms eg.Parasite and fungi

*There are two types of organelles :

**-Membranous organelles like :**

- Mitochondria
- Nucleus
- Endoplasmic reticulum (ER)
- Golgi apparatus
- Lysosomes
- Peroxisomes

**-Non-membranous organelles :**

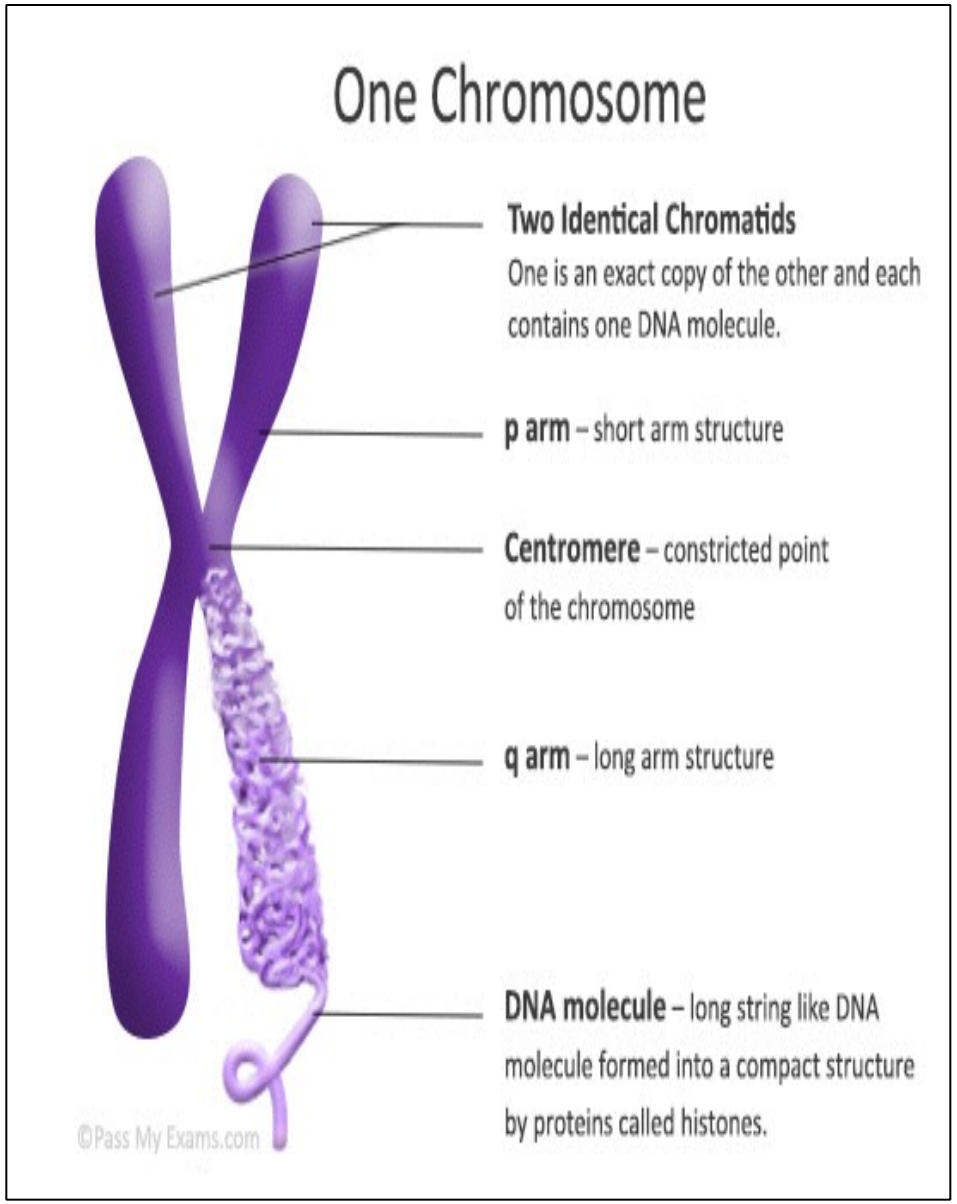
- Cytoskeleton
- Microvilli
- Centrioles
- Cilia
- Flagella
- Ribosomes

# Chromosomes:

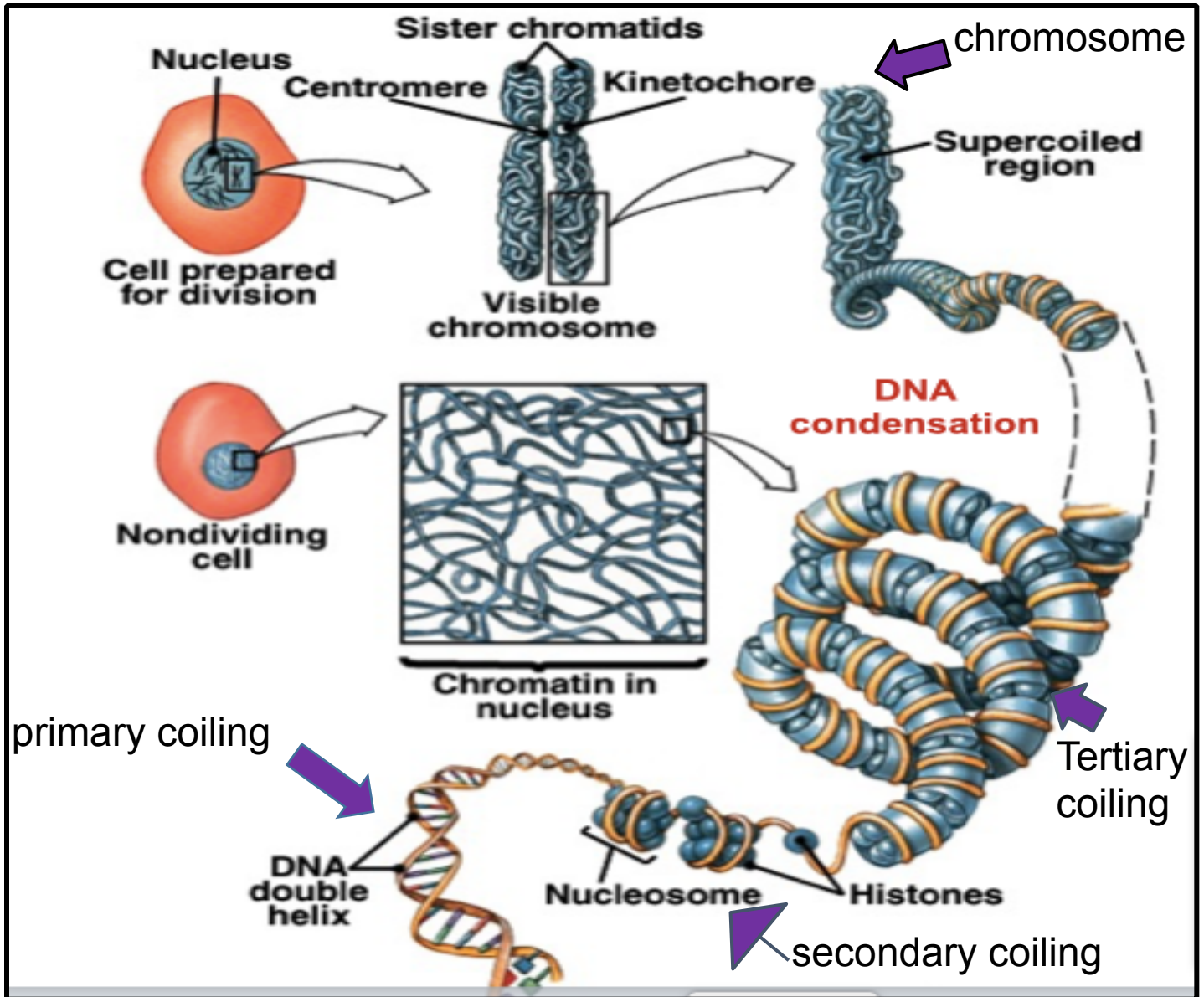
**1- carry genetic material** (On the form of DNA)

**2-heredity: each pair of homologues consists of one paternal and one maternal chromosome**

**3- The intact set is passed to each daughter cell at every mitosis**



# The Structure of chromosome:




**Order Of DNA coiling and folding :**

1-Primary coiling: DNA double helix.
2-Secondary coiling: around histones (basic proteins) nucleosomes
3-Tertiary coiling: chromatin fiber
-Chromatin fibers form long loops on non-histone proteins tighter coils chromosome.

*folding the protein makes it active
*The histones are positively charged the DNA is negatively charged

Chromosome structure:
https://www.youtube.com/watch?v=zf7tbymrv9o

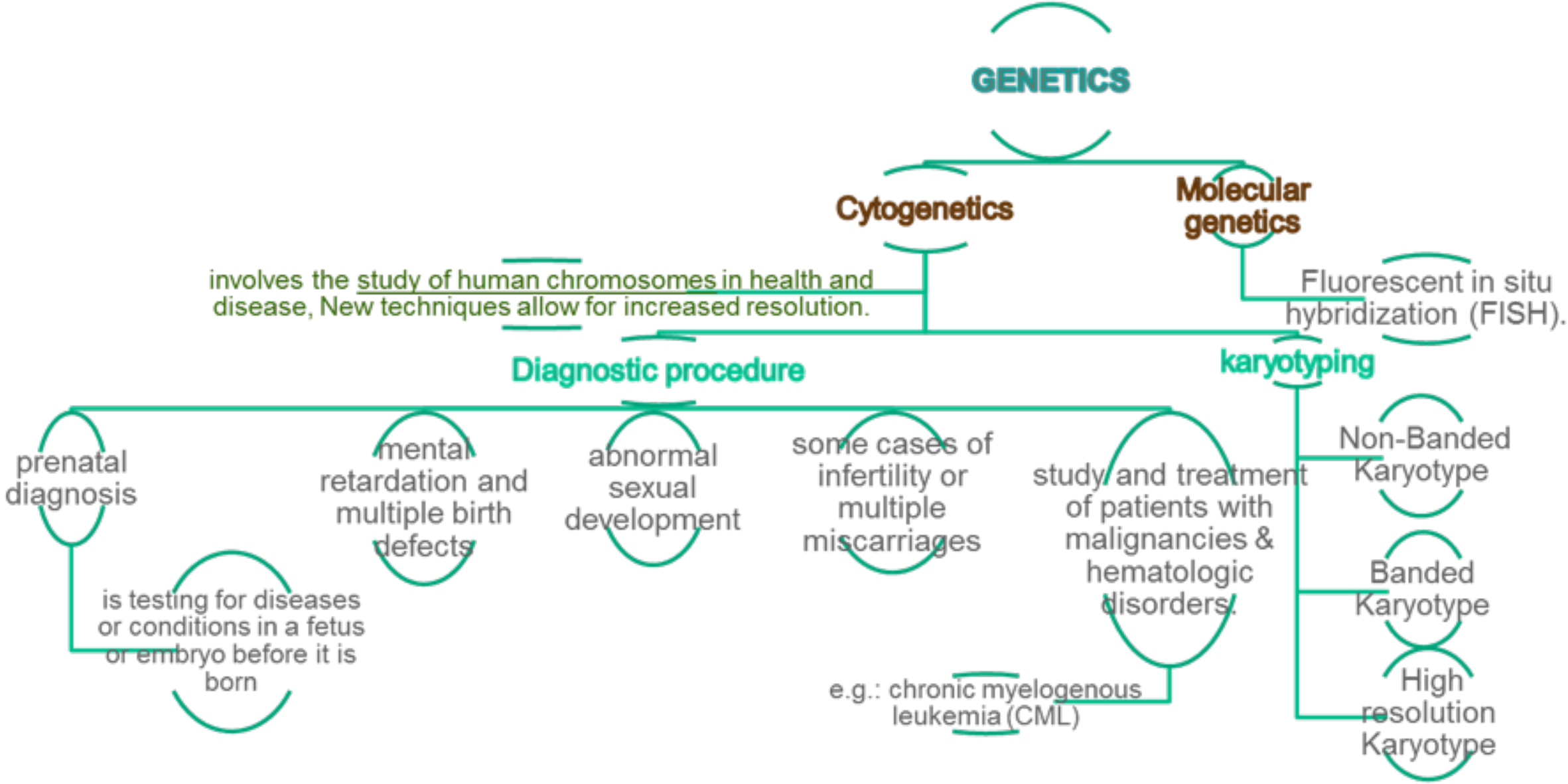
# Genes

- **Cytogenetics:**

The study of the structure and function of chromosomes and chromosome behaviour during somatic and germline division

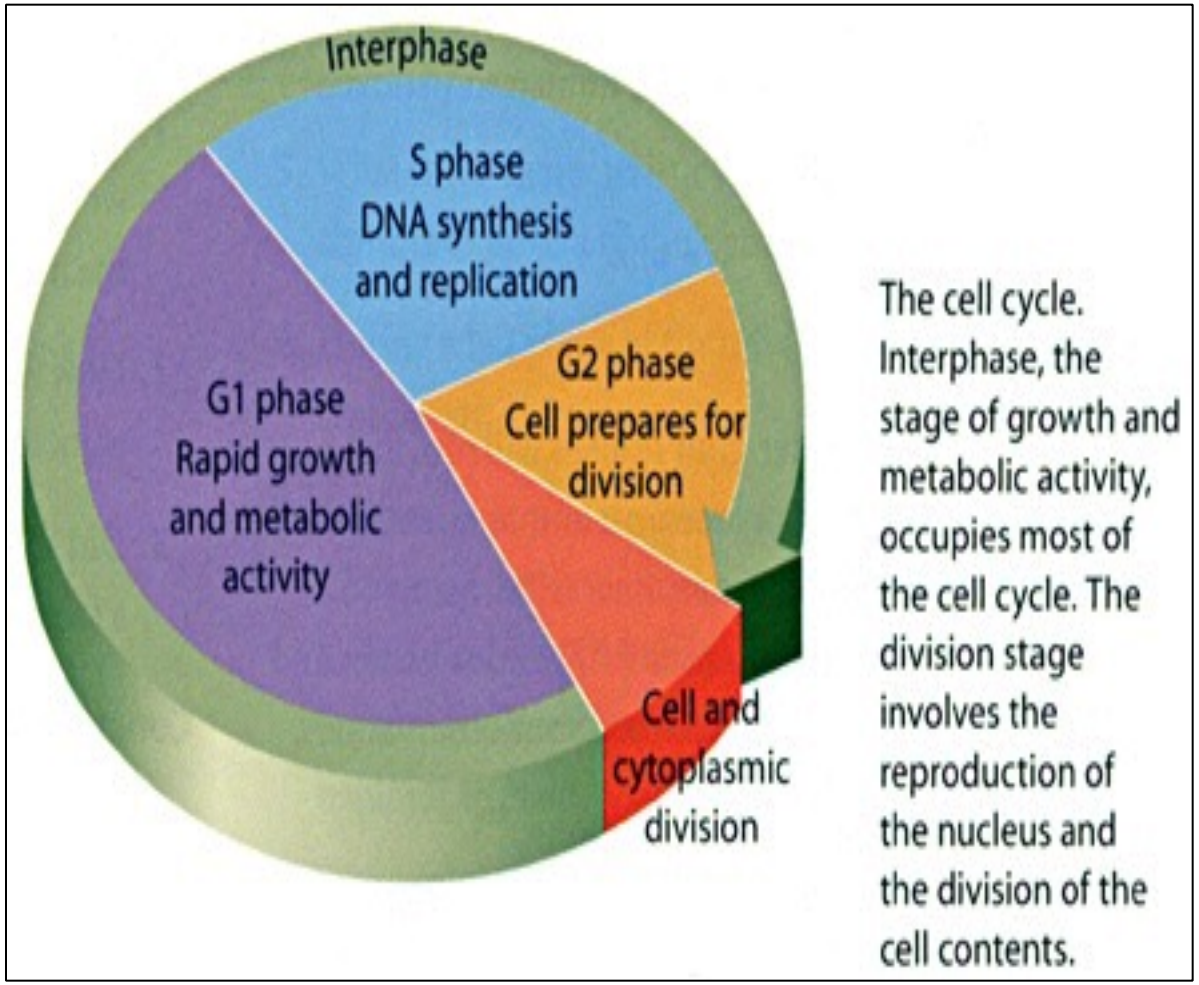
- **Molecular genetics:**

The study of the structure and function of genes at a molecular level how the genes are transferred from generation to generation


GENETICS
Cytogenetics
Molecular genetics
involves the study of human chromosomes in health and disease, New techniques allow for increased resolution.
Fluorescent in situ hybridization (FISH).
Diagnostic procedure
karyotyping
prenatal diagnosis
is testing for diseases or conditions in a fetus or embryo before it is born
mental retardation and multiple birth defects
abnormal sexual development
some cases of infertility or multiple miscarriages
study and treatment of patients with malignancies & hematologic disorders.
e.g.: chronic myelogenous leukemia (CML)
Non-Banded Karyotype
Banded Karyotype
High resolution Karyotype

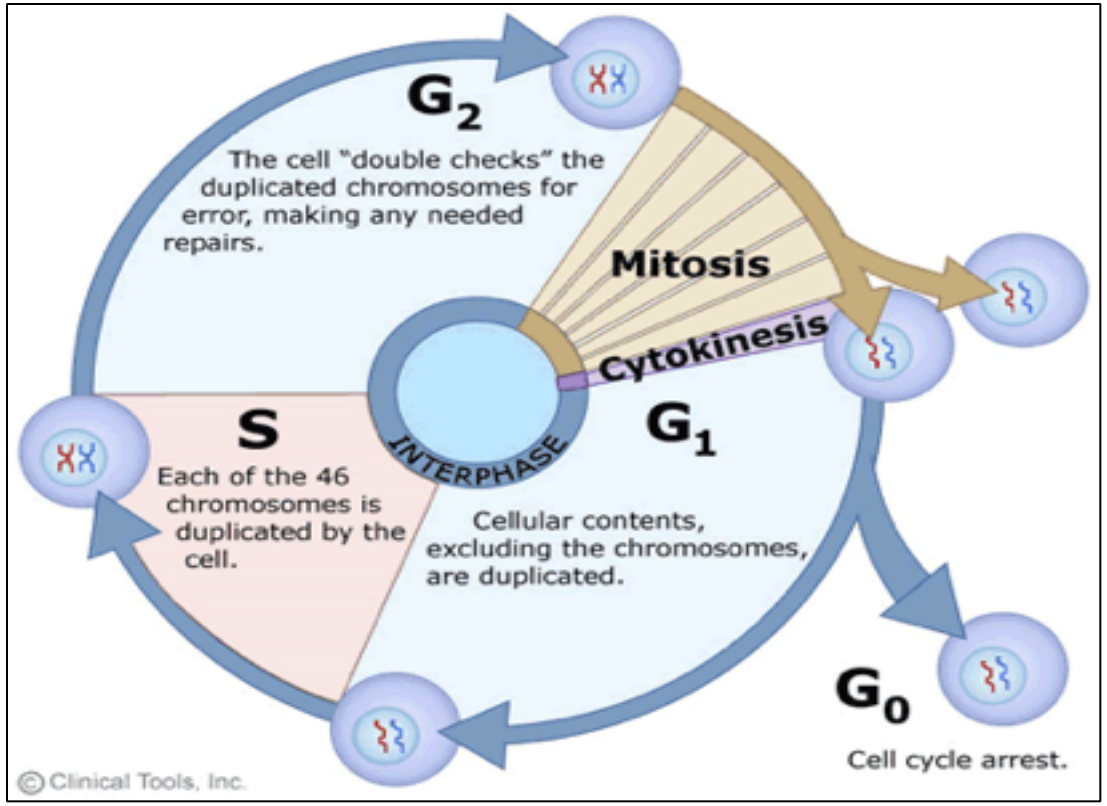
# Mitotic cell cycle

*Interphase is the longest stage*




The cell cycle. Interphase, the stage of growth and metabolic activity, occupies most of the cell cycle. The division stage involves the reproduction of the nucleus and the division of the cell contents.

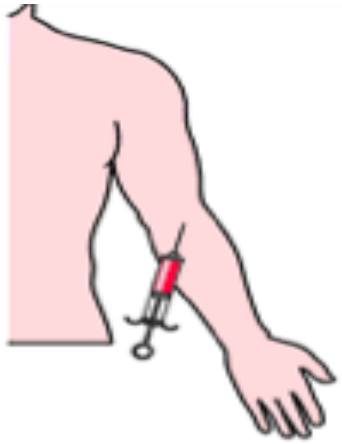
**G1 Phase :** It takes about 10-12 hrs (Growth and normal metabolic activity)
**S Phase :** It takes about 6-8 hrs (DNA replication)
**G2 Phase :** It takes about 2-4 hrs (Preparation for mitosis)
**Mitotic Phase :** Prophase, Metaphase, Anaphase and Telophase



# Procedure of Chromosome Preparation from Peripheral Blood

Trypsin : An enzyme that removes the proteins .

*know the order of the steps



5 mL venous blood

Add phytohemagglutinin and culture medium

Culture media contains Phytohemagglutinin to stimulate T lymphocytes to divide

Culture at 37°C for 3 days

Prevents formation of the spindle → arrest cell division during metaphase

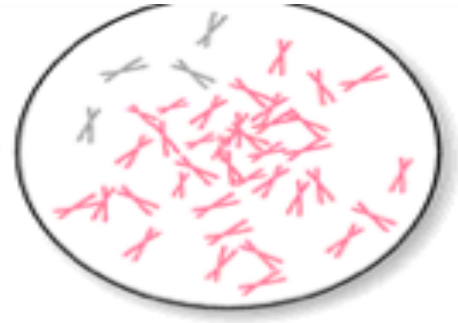
Add colchicine and hypotonic saline

Cells fixed

Spread cells onto slide by dropping

Digest with trypsin and stain with Giemsa

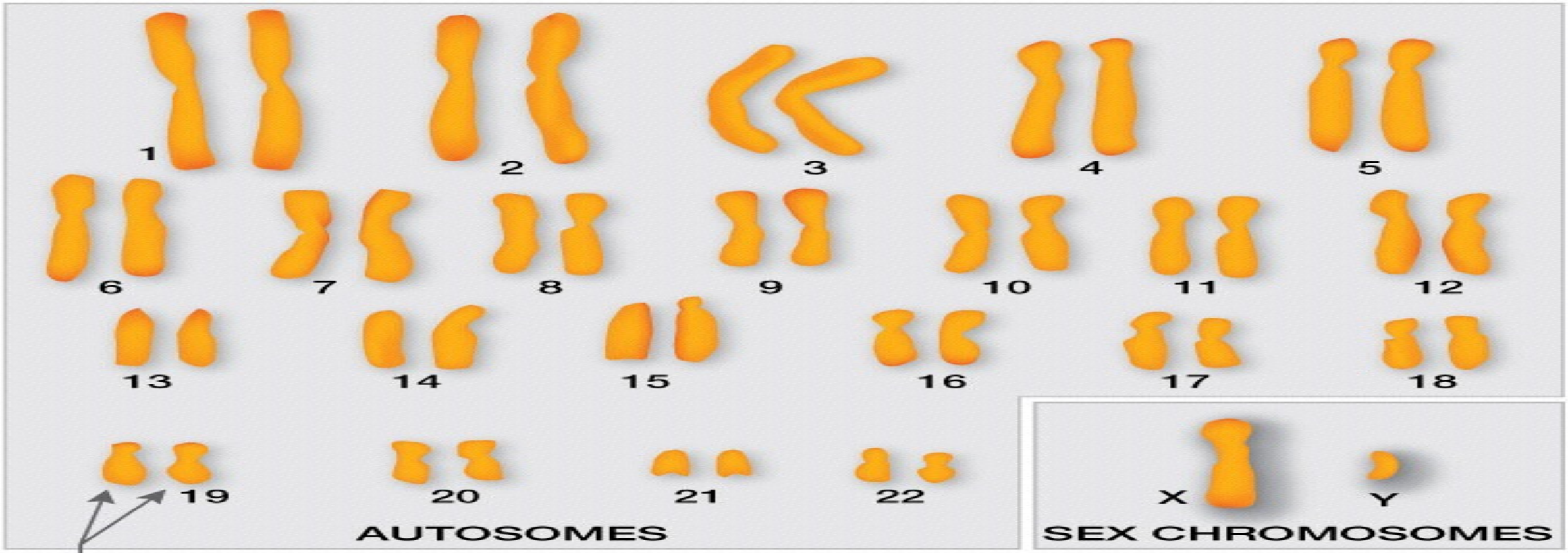
Analyze "metaphase spread"



Karyotype

A visual demonstration for Karyotyping:
https://youtu.be/7ShPzzrCetE

# KARYOTYPE : The number and appearance of chromosomes in the nucleus of a eukaryotic cell




Pair of homologous chromosomes:

- *One from mom and one from dad*
- *Have the same genes arranged in the same order*
- *Slightly different DNA sequences*

# Karyotyping

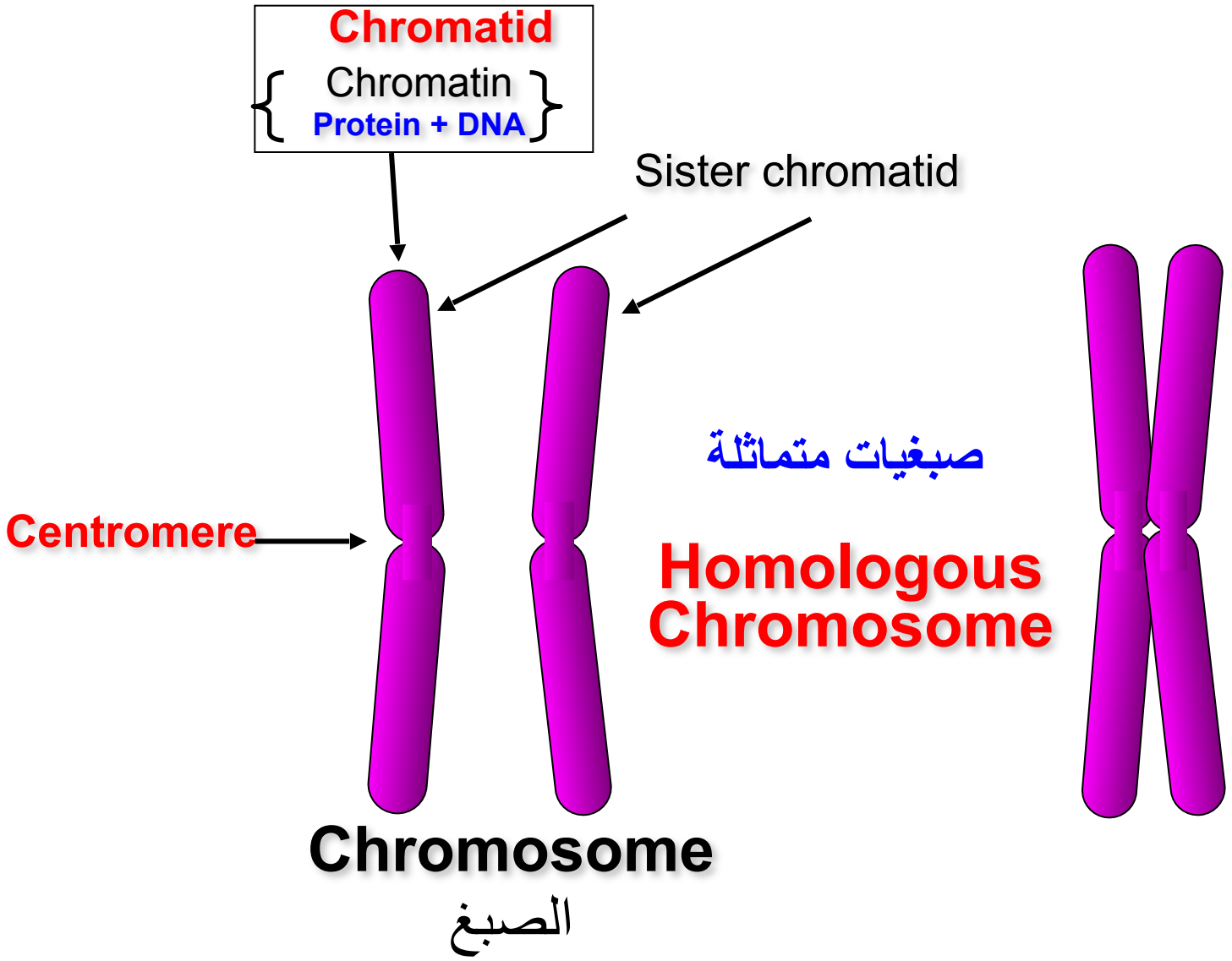
## *Based on:*

1_ the length

2_ the position of the centromere

3_ the presence or absence of satellites

The kinetochore can adhere the chromosomes to the spindle fibers . the length of the chromosome does NOT mean that the chromosome is going to have more GENES.

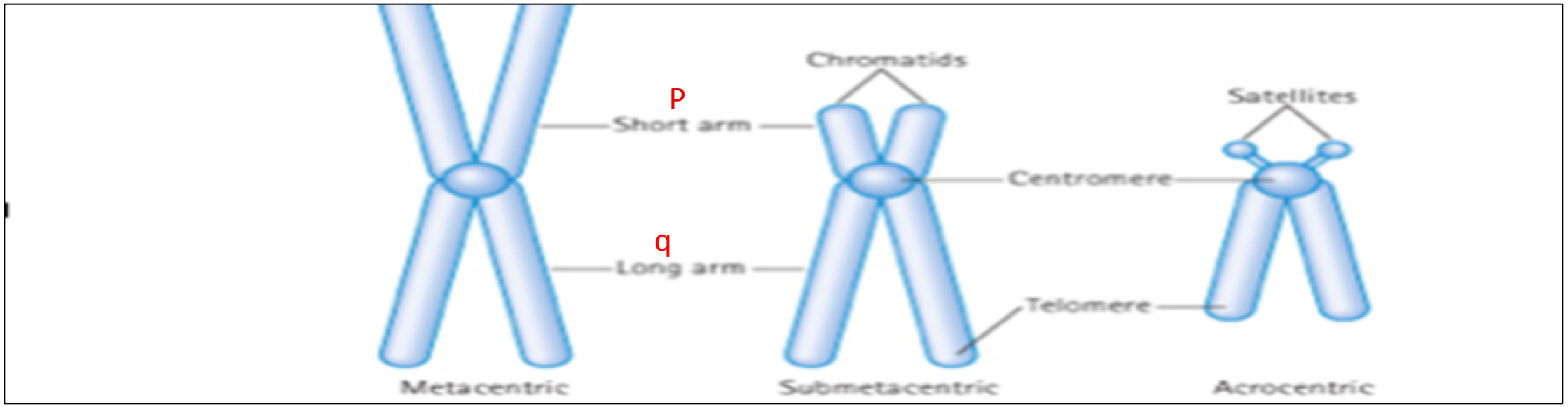


# Karyotype:

A series of steps involved :

1-Culturing
2-Harvesting
3-Slide-Making
4-Banding
5-Staining
6-Karyotyping
7-Chromosome Analysis

# Centromeric position and arm length




The ratio of the lengths of the two arms is constant for each chromosome. This ratio is an important parameter for chromosome identification and allows classification of chromosomes into several basic morphologic types:

**i-*metacentric*** **ii-*sub-metacentric*** **iii-*acrocentric***

In the human karyotype chromosome pairs 13, 14, 15, 21, 22 are *acrocentric*

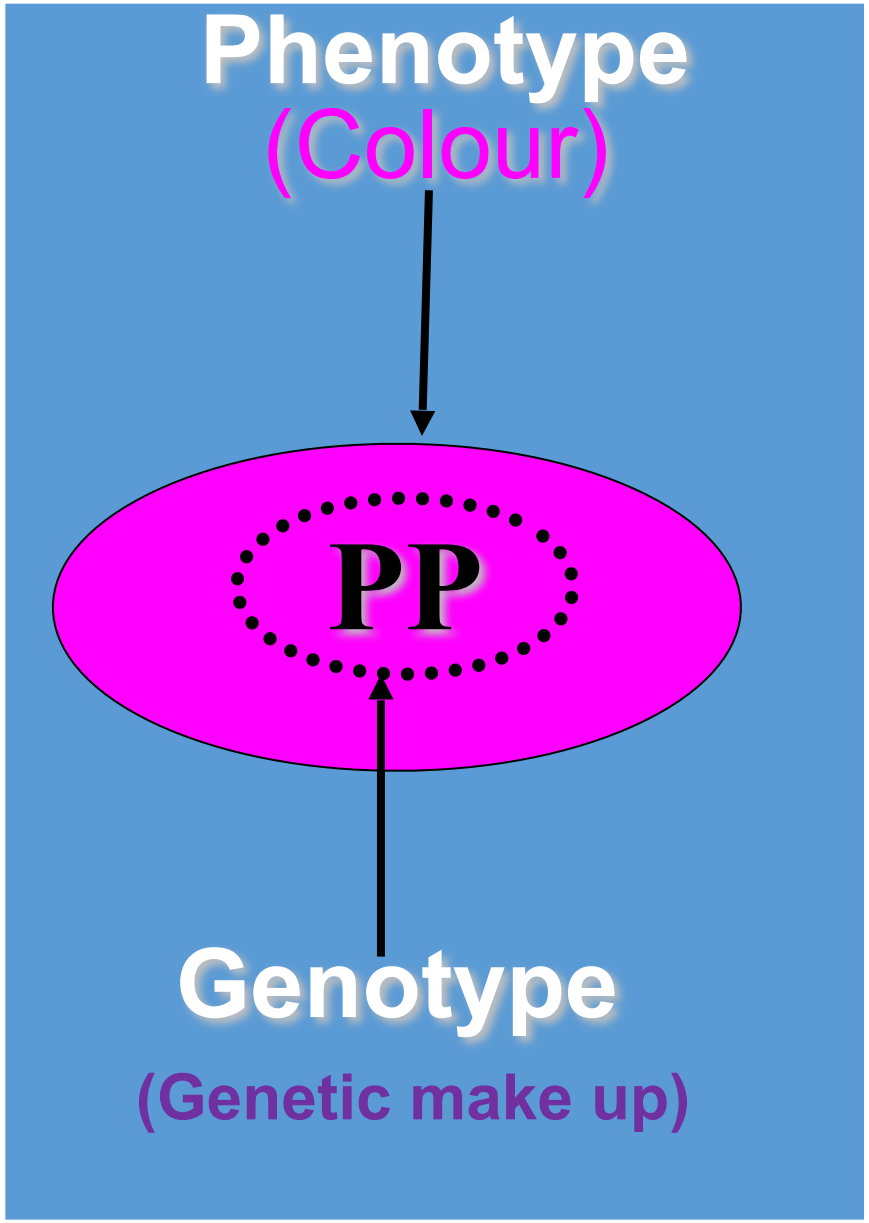
# Metaphase chromosomes:

- The 2 sister-chromatids
are principally held together at the centromeric region.

- Each chromosome has a centromere (CEN),
region which contains the kinetochore,

- CEN divides the chromosome into two arms:
the short arm (p arm) and the long arm (q arm).

- Each arm terminates in a telomere.

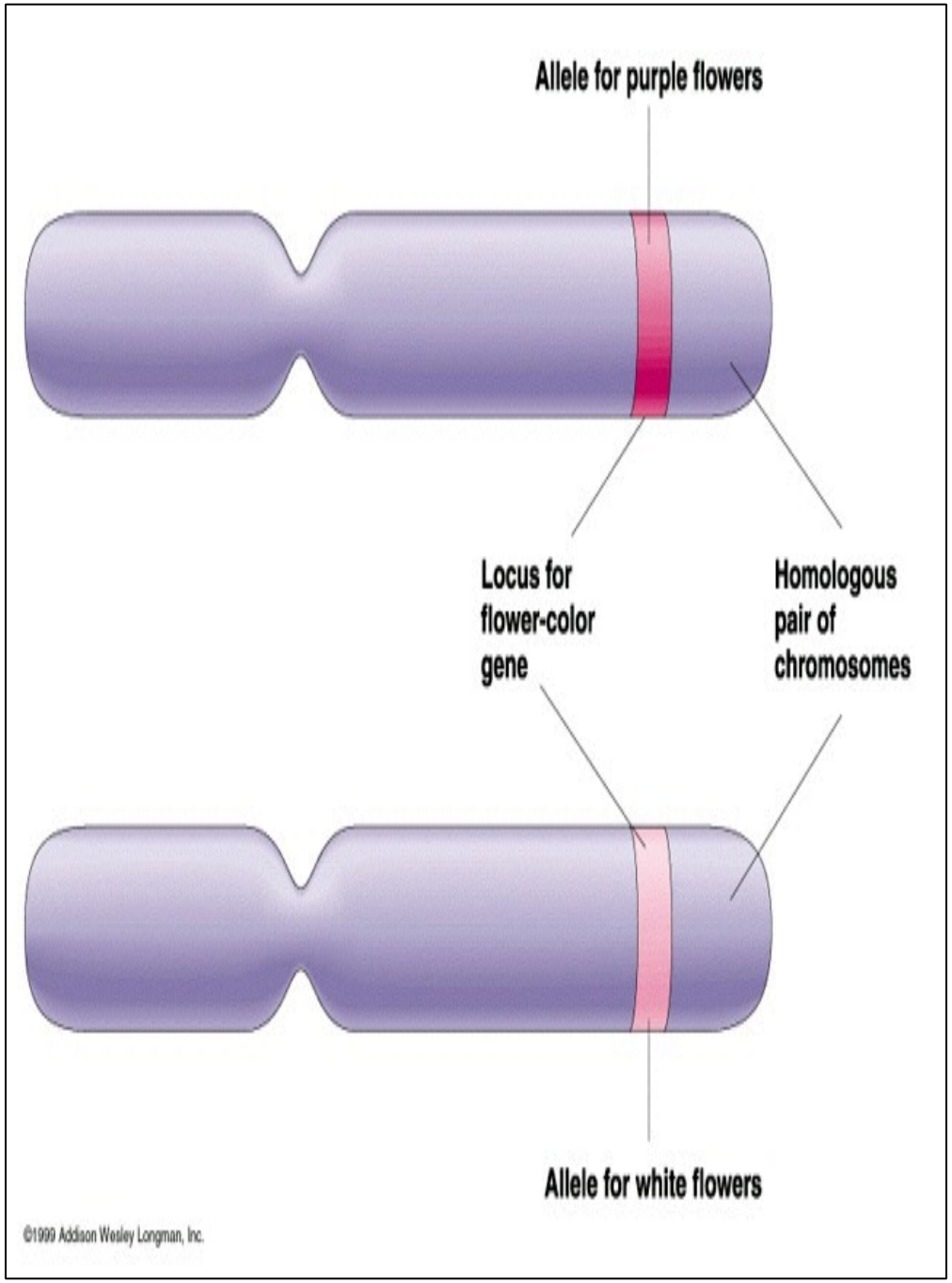



**Genotype:**

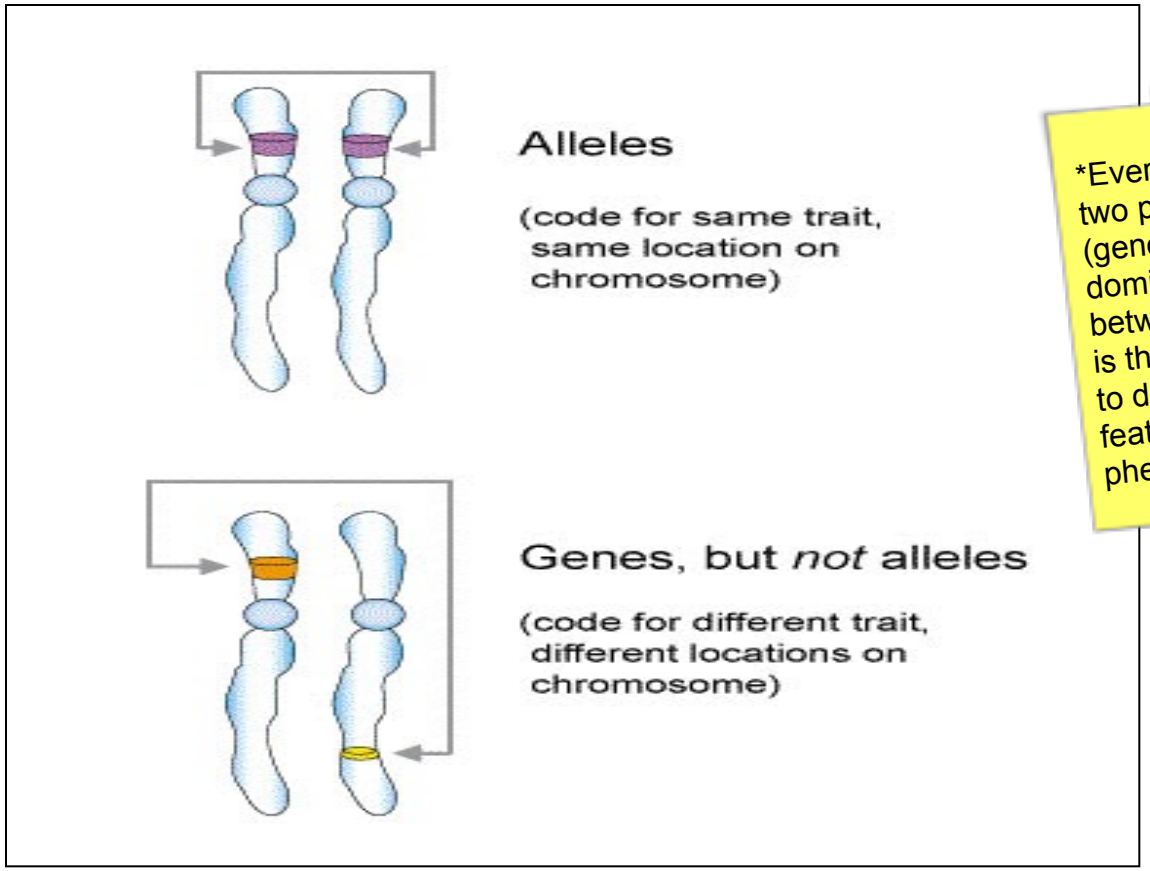
Genetic constitution of a cell, an organism, or an individual, that is the specific allele makeup of the individual

**Phenotype:**

A phenotype is any observable characteristic of an organism, such as its morphology, development, biochemical or physiological properties, or behavior




**Alleles:** One of the alternative versions of a gene at a given location (locus) along a chromosome.
An individual inherits two alleles from each parent.




*Every phenotype has two parallel alleles (genotype), the dominant allele between the two alleles is the one that is going to determine the features of this phenotype.

**The human albino gene has two allelic forms,**
**Dominant A and Recessive a .**
**So, there are three possible genotypes :**

Cross: Aa x Aa

| | A | a |
|---|---|---|
| A | AA | Aa |
| a | Aa | aa |

AA : Homozygous dominant.
Aa : Heterozygous .
aa: Homozygous recessive.

## Chromosomal classification :

22 pairs Autosomes, from 1 – 22 by order of decreasing length.
1 pair of sex chromosomes:
XX for FEMALE.
XY for MALE.

## Items in the description of Karyotype:

Normal Karyotypes:
46,XY
46,XX
Abnormal karyotypes:
47,XY,+21
45,XY

# Banding

❖Certain staining techniques cause the chromosomes to take on a banded appearance

❖Each arm presenting a sequence of dark and light bands .

❖Patterns are specific and repeatable for each chromosome,

❖Allowing accurate identification and longitudinal mapping for locating gene positions and characterising structural changes.

❖Patterns, and the nomenclature for defining positional mapping have been standardised .

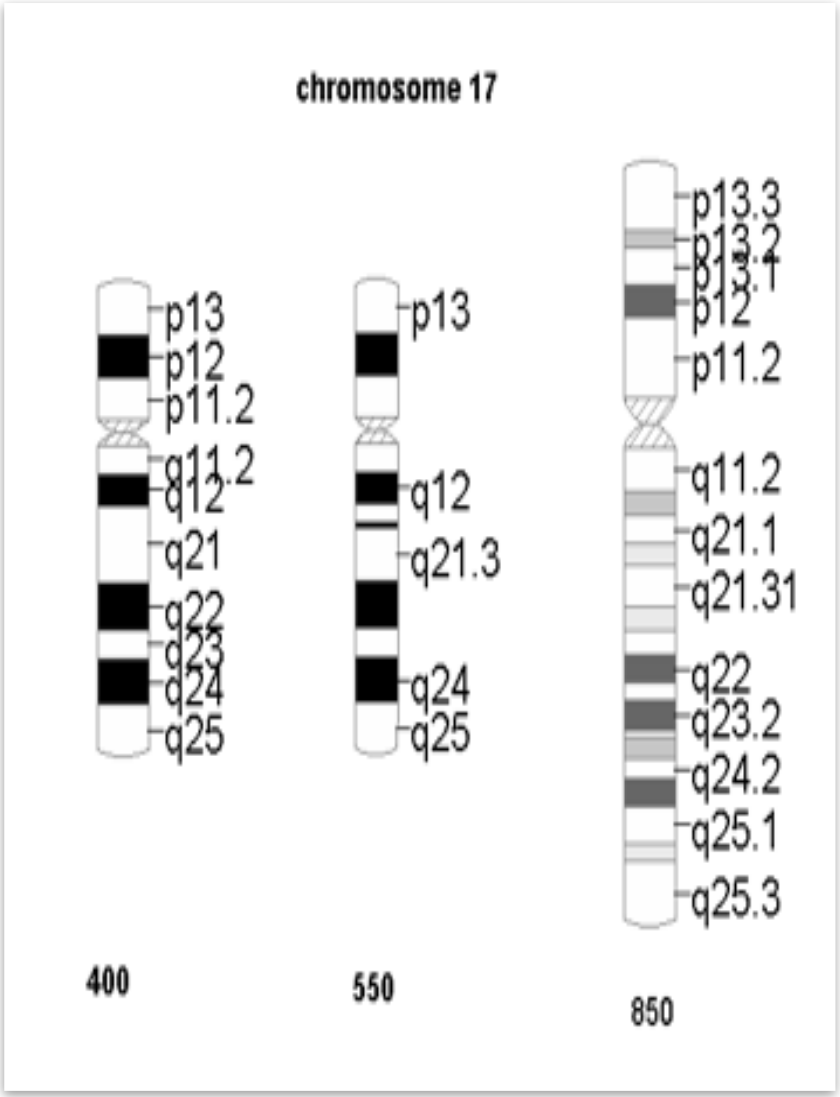
*In the nomenclature of the bands, we should start from the centromere.(P) is used in naming the shorter segment, (Q) is used in naming the longer one

# Chromosome Banding

**Band resolution =**

**Estimate of number of light + dark bands per haploid set of chromosomes.**

**More Numbers » More Resolution**
**400 » 550 » 850**



# Chromosome Banding:

**G** = Giemsa
**R** = Reverse (revers of G-bands)
**Q** = Quinicrine.
**C** = Centromeric heterochromatin.

## G Banding:

**Treat with trypsin and then with Geimsa Stain.**

## R Banding:

**heat and then treat with Geimsa stain.**

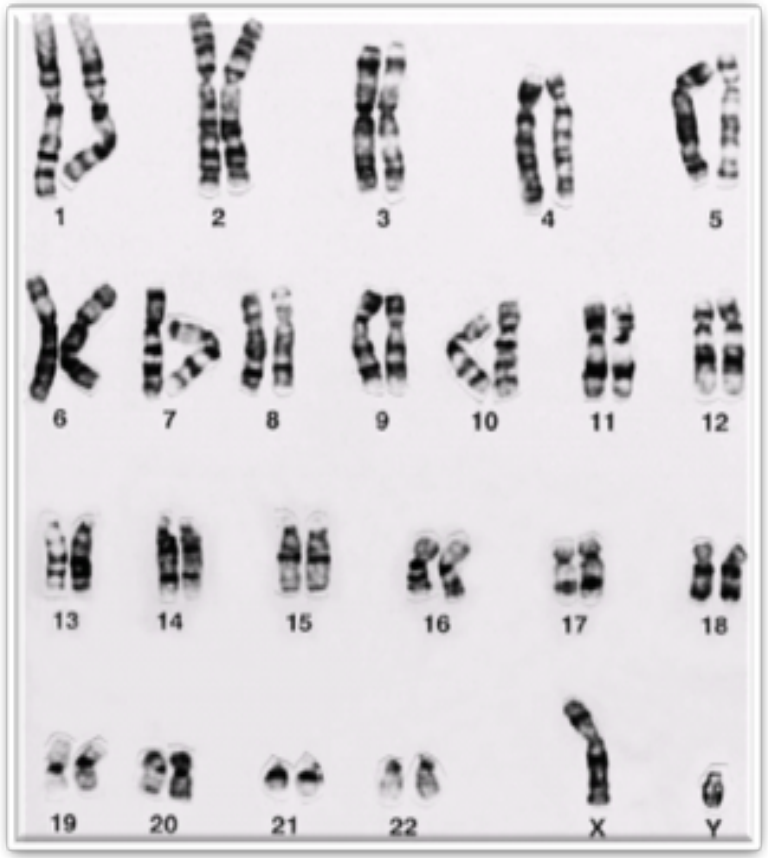
## Q Banding:

**Treat with Quinicrine dye giving rise to fluorescent bands. It requires an ultraviolet fluorescent microscope.**

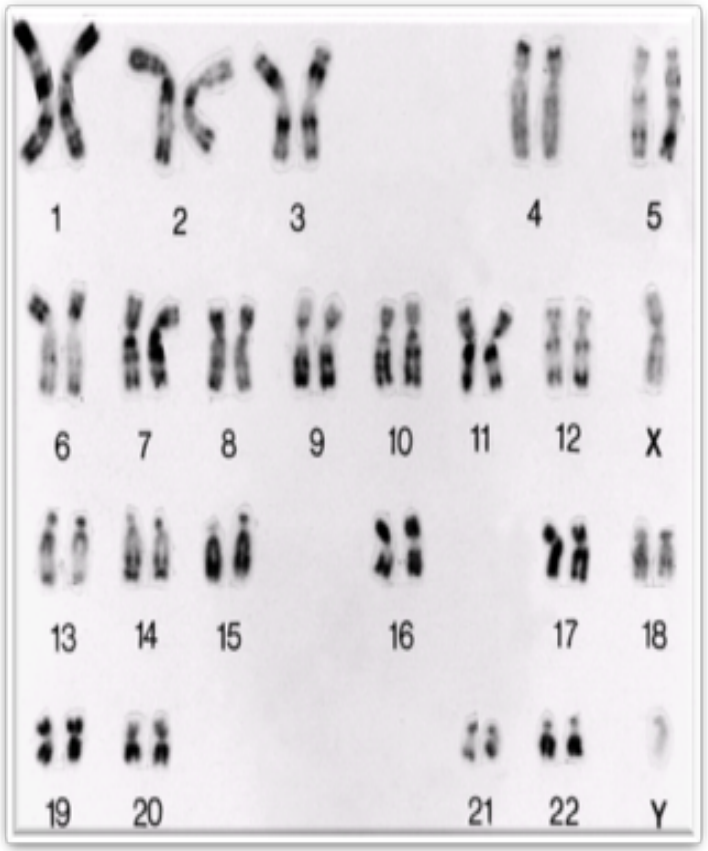
## C Banding:

**Staining of the Centromere. Treat with acid followed by alkali prior to G banding.**

# Banded Karyotype:
# Normal Banded Karyotypes :




A normal G-banded male Karyotype

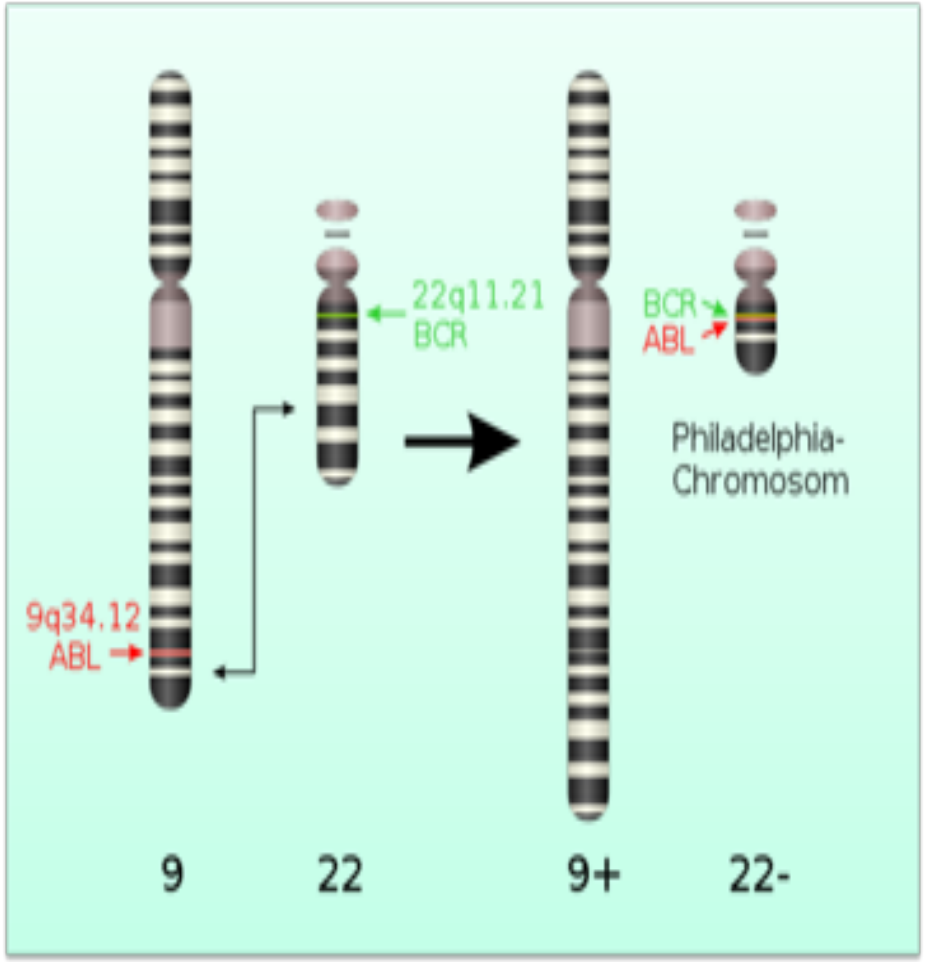



A normal R-banded male Karyotype

# Philadelphia-chromosome translocation

Critical genetic event in the development of CHL(chronic myelogenous leukemia).

Due to a cytogenetic abnormality (translocation between 9 and 22).

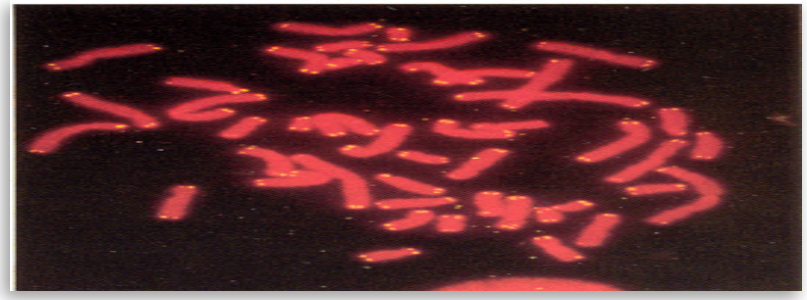


# Fluorescence In-Situ Hybridization (FISH)

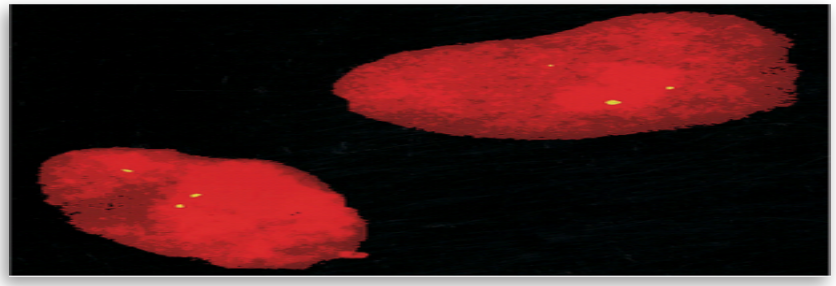
- Using Fluorescent probe that binds with its complementary target sequence.
- They can be to study chromosomes in metaphase or interphase.

The hybridization occurs between one of the DNA's strands and the probe.
***Aneuploidy :** An abnormal number of chromosomes.

**Usage :** to determine chromosomal abnormalities, e.g. mutations, aneuploidy, .



**FISH of metaphase with a probe for telomere showing signals at the end of each chromatid**



**FISH of interphase nuclei with a chromosome 21 centromeric probe showing 3 signals consistent with trisomy 21**

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لا تسكن بلداً لا يكون فيه عالم يفتيك في دينك ولا طبيب ينبئك عن أمر بدنك..
الشافعي