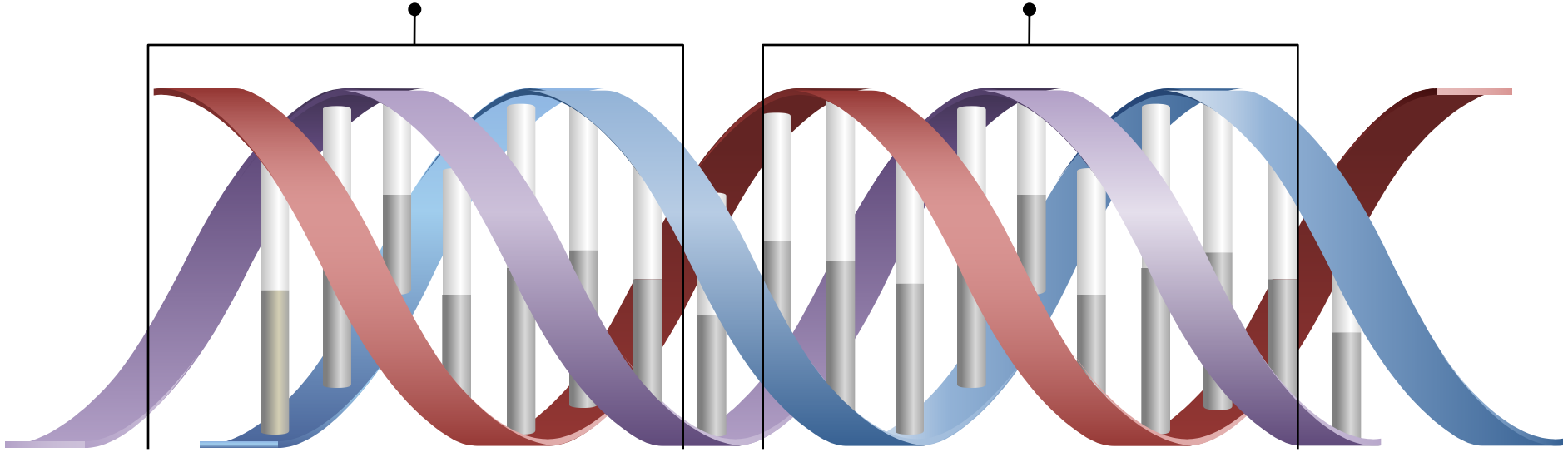
جامعة الملك سعود
King Saud University

Human Genetics 439

Lecture 1

Human chromosomes



Index color:

- Important
- Slides
- Notes
- Extra information

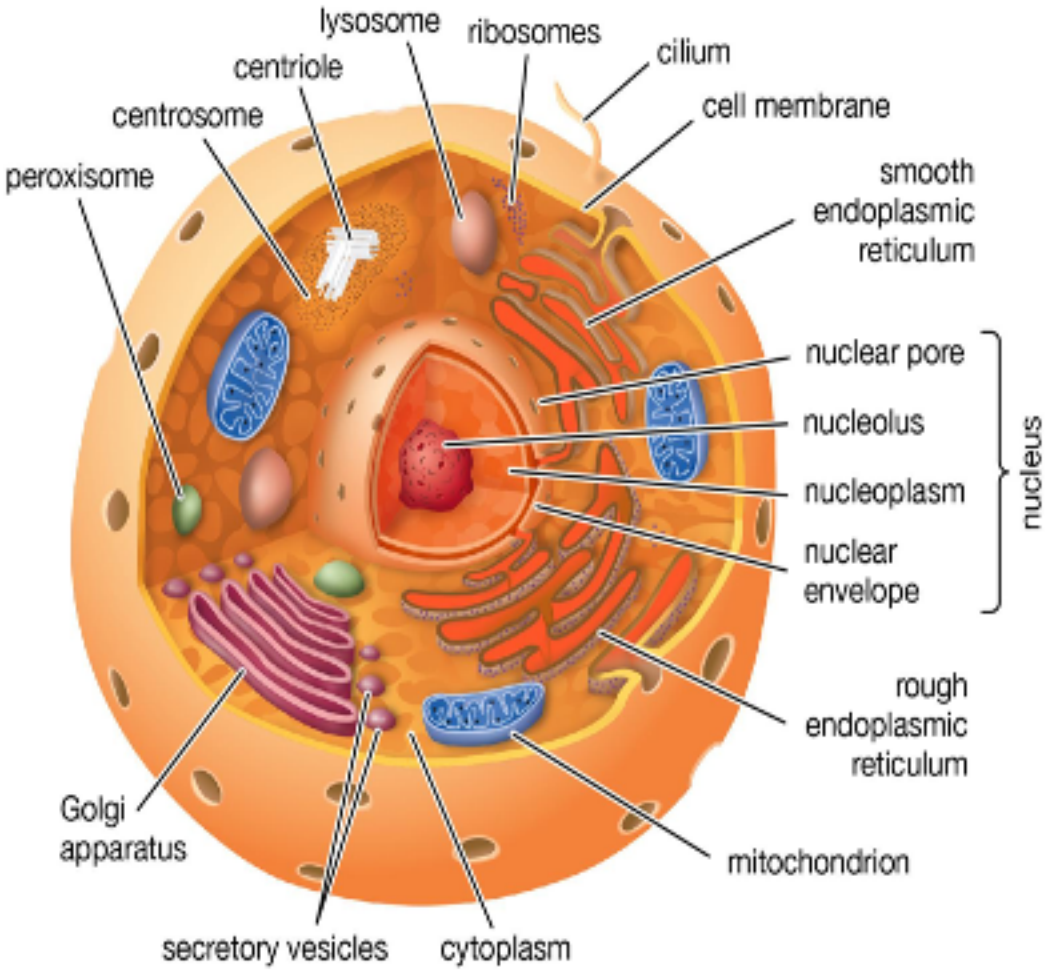
MED439

Objectives:

By the end of the lecture, the student should:

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

Eukaryotic cell



The Nucleus + Cell Control

- The **nucleus** is the leader of the eukaryotic cell because…
  - **It contains the directions to make proteins**
    - *Proteins are needed by every part of the cell*
- **Chromatin**
  - Strands of DNA
  - When a cell divides, chromatin condenses into **chromosomes**

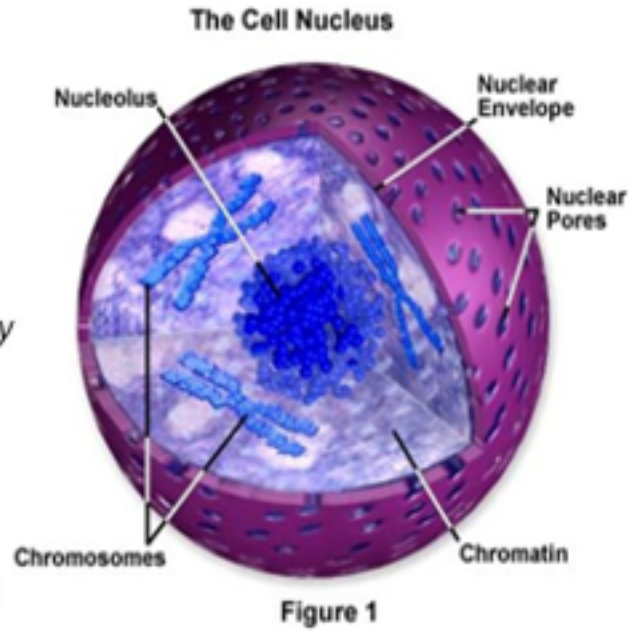


Figure 1

Genetics

Cytogenetics
(cell level)

The study of structure and function of **chromosomes** and their behaviour during somatic and germline division.

↓

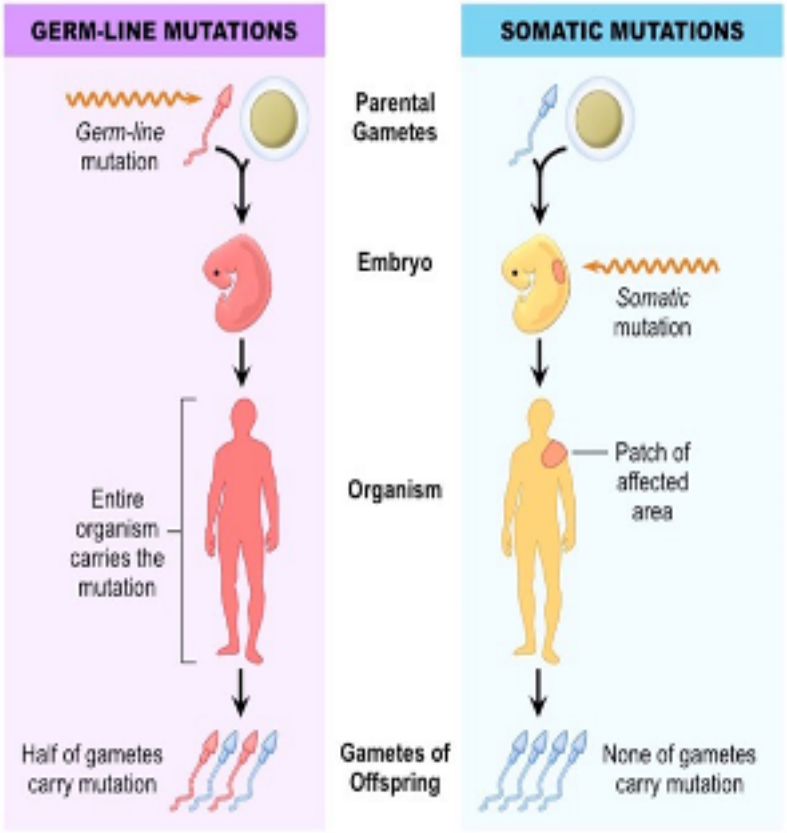
- Non-Banded karyotype
- Banded karyotype
- High resolution karyotype

Molecular genetics
(Molecular level)

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

↓

- Fluorescent in situ hybridization (**FISH** 🐟)



Note:When a mutation occurs within germ cells, it is called germline mutation. Germline mutations affect every cell in an organism and are passed onto offspring. When a mutation occurs in a somatic cell, it is called a somatic mutation .

CYTOGENETICS

Human cytogenetics: The study of human chromosomes in health and disease.

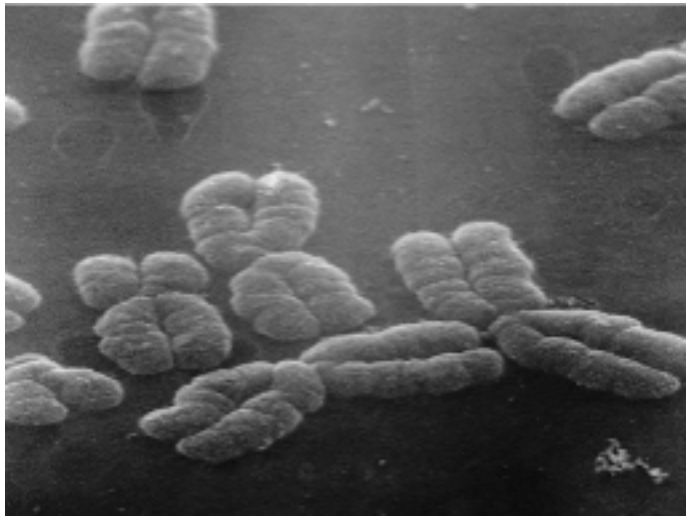
Chromosome studies are an important laboratory diagnosis in:

- Prenatal diagnosis
- Certain patients with mental retardation and multiple birth defects
- Patients with abnormal sexual development
- Some cases of infertility or multiple miscarriages
- In the study and treatment of patients with malignancies and hematologic disorders

CHROMOSOMES:

Note:Genes are transmitted to daughter cells while they are loose (decondensed)

- Carry genetic material
- Heredity: each pair of homologues consists of one paternal and one maternal chromosome.
- The intact set is passed to each daughter cell at every mitosis.



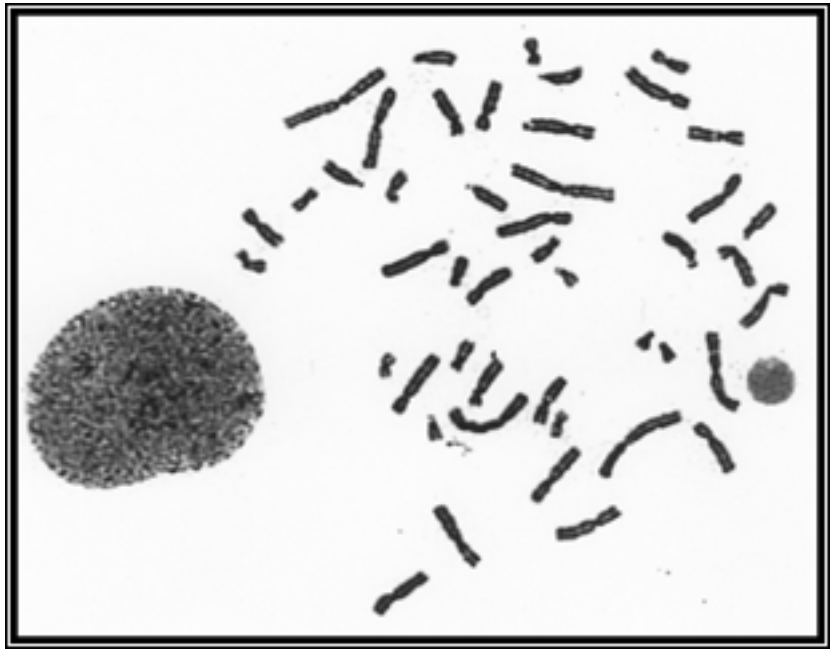
Electron Microscope(EM) OF HUMAN CHROMOSOMES

CHROMOSOMAL CLASSIFICATION:

-22 pairs of **autosomes**, numbered from 1 to 22 by decreasing length

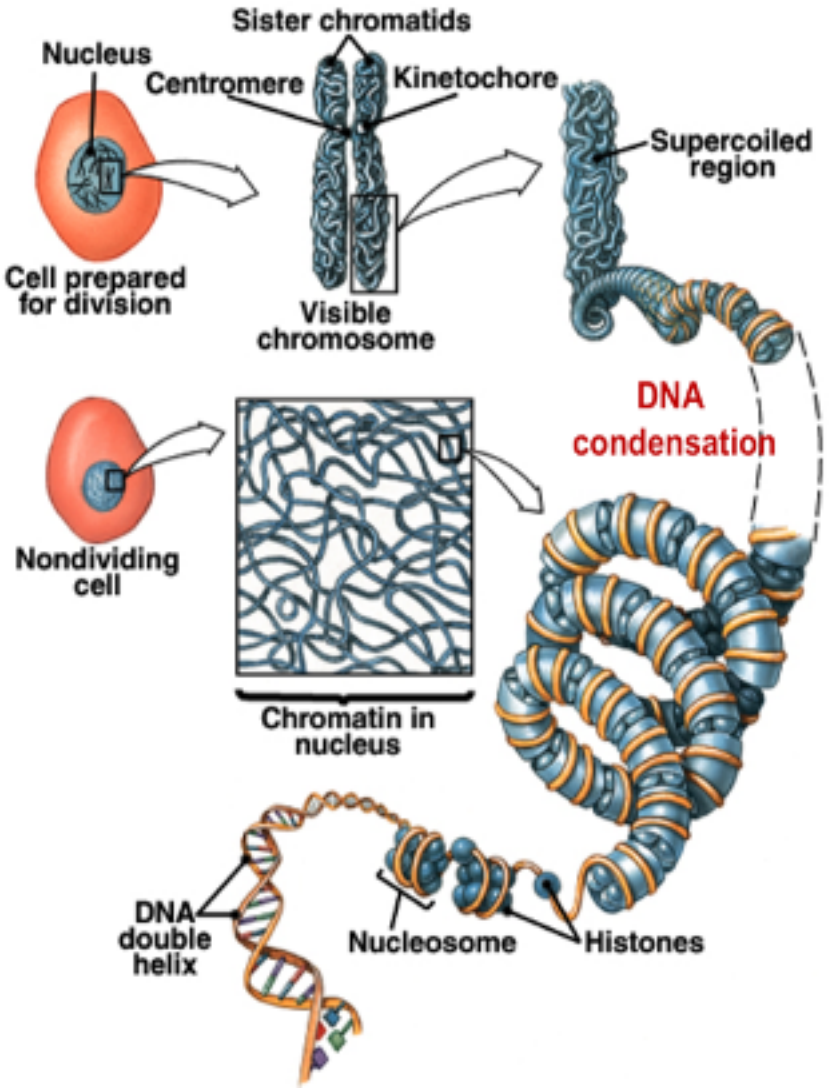
-1 pair of **sex** chromosomes:
XX in the female,
XY in the male.

Human Chromosomes:

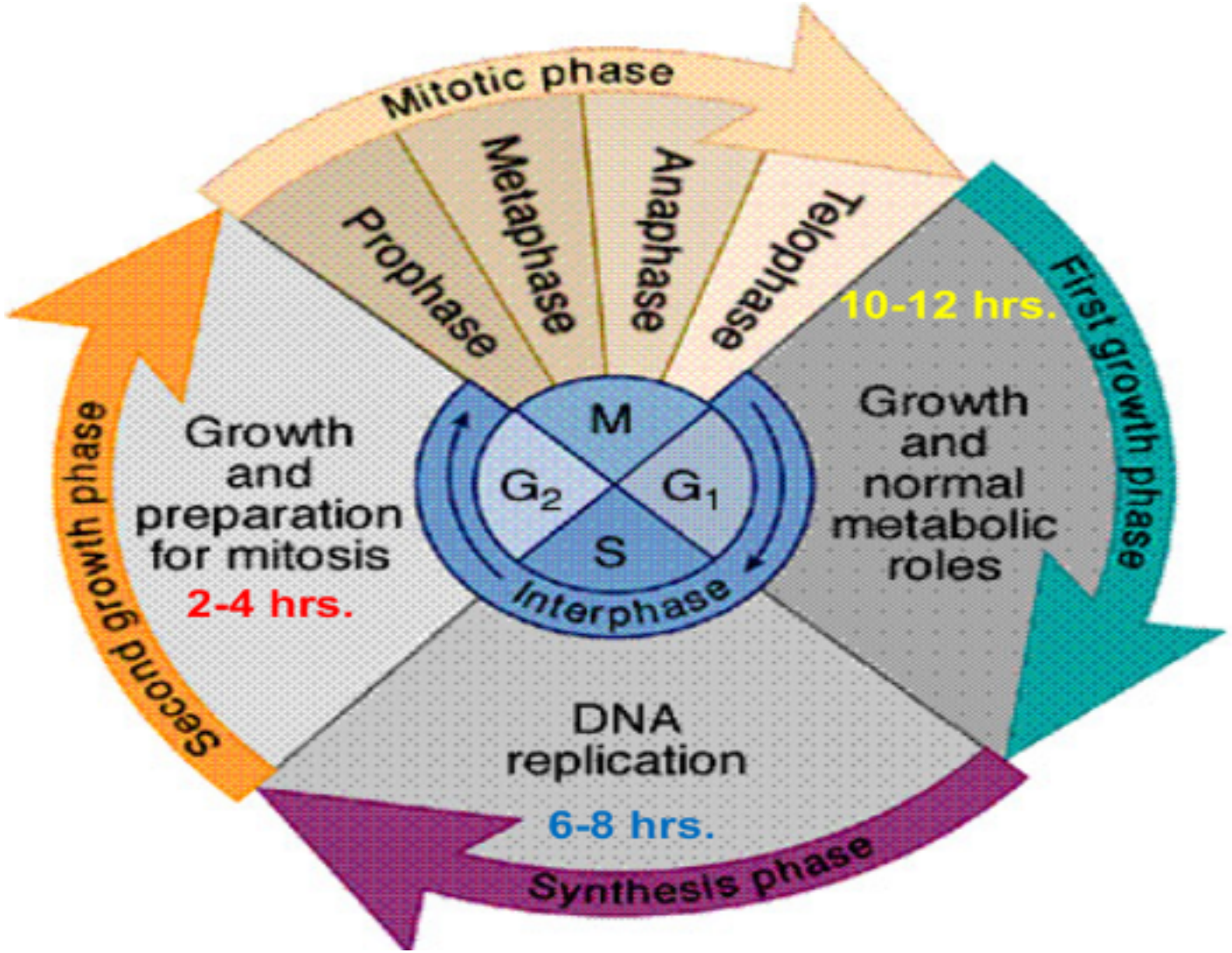


STRUCTURE OF CHROMOSOME

- Primary coiling : **DNA double helix**
- Secondary coiling : around histones (basic protiens) > **nucleosomes**
- Tertiary coiling : **chromatin fiber**
- Chromatin fibers form long loops on non-histone protien > tighter coils > **chromosomes**



MITOTIC CELL CYCLE :



METAPHASE CHROMOSOMES:

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

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

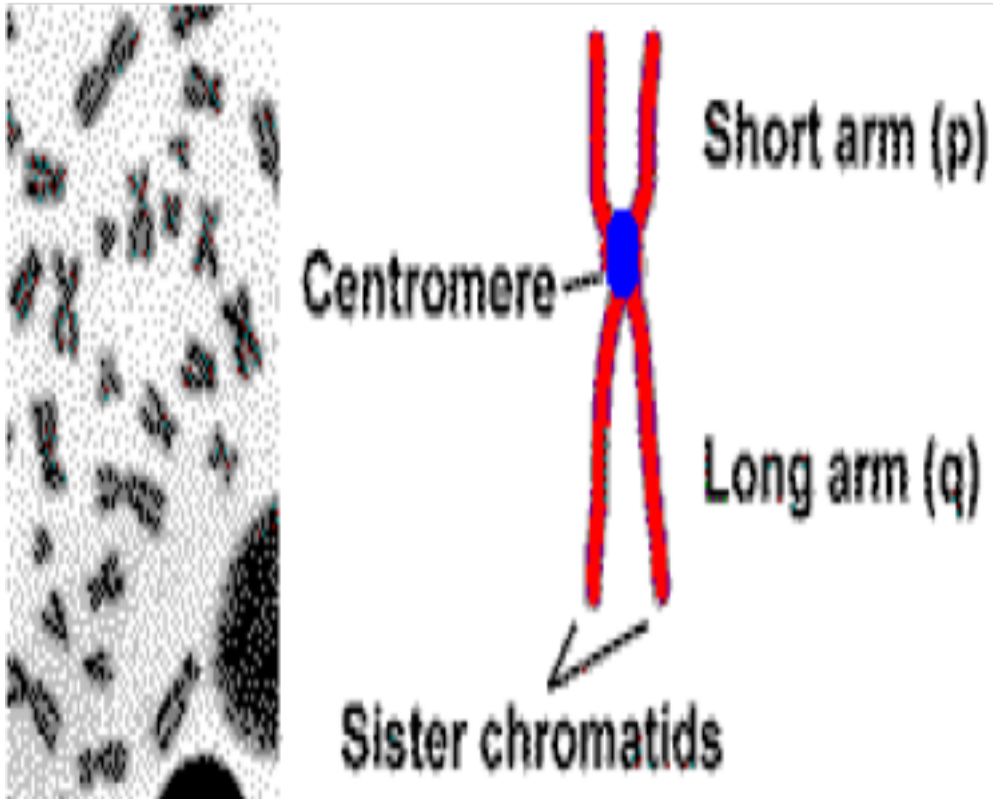
-CEN divides the chromosome into two arms

1-short arm (P arm)

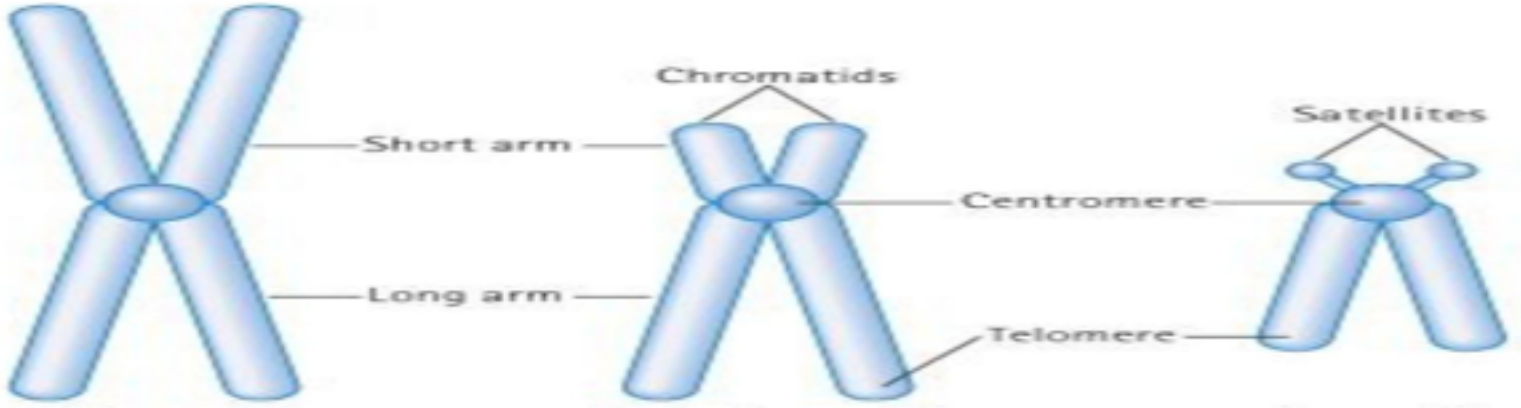
2-long arm (Q arm)

- Each arm terminates in a **telomere.**

A single complete set of chromosomes. (N=23 for humans)



CENTROMERIC POSITION AND ARM LENGTH:



1 2 3

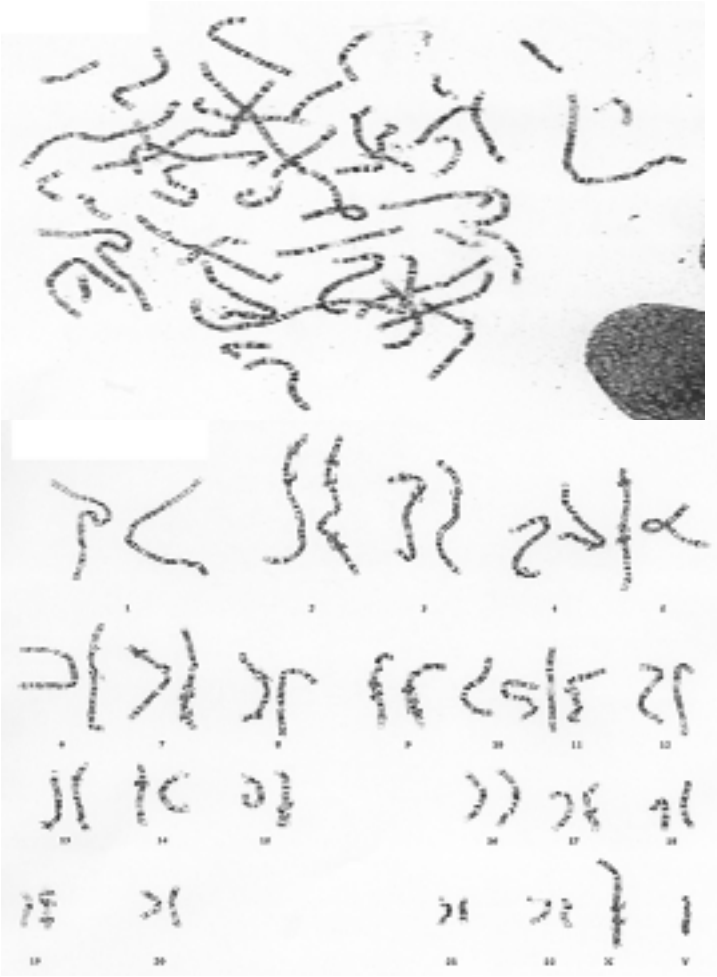
- The ratio of the lengths of the two arms is **constant** for each chromosome.
- This ratio is an important parameter for chromosome identification and allows classification of chromosomes into several basic morphologic types:
- 1-metacentric
- 2-sub-metacentric
- 3-acrocentric
- In the human karyotype chromosome pairs 13, 14, 15, 21, 22 are acrocentric.

KARYOTYPE:

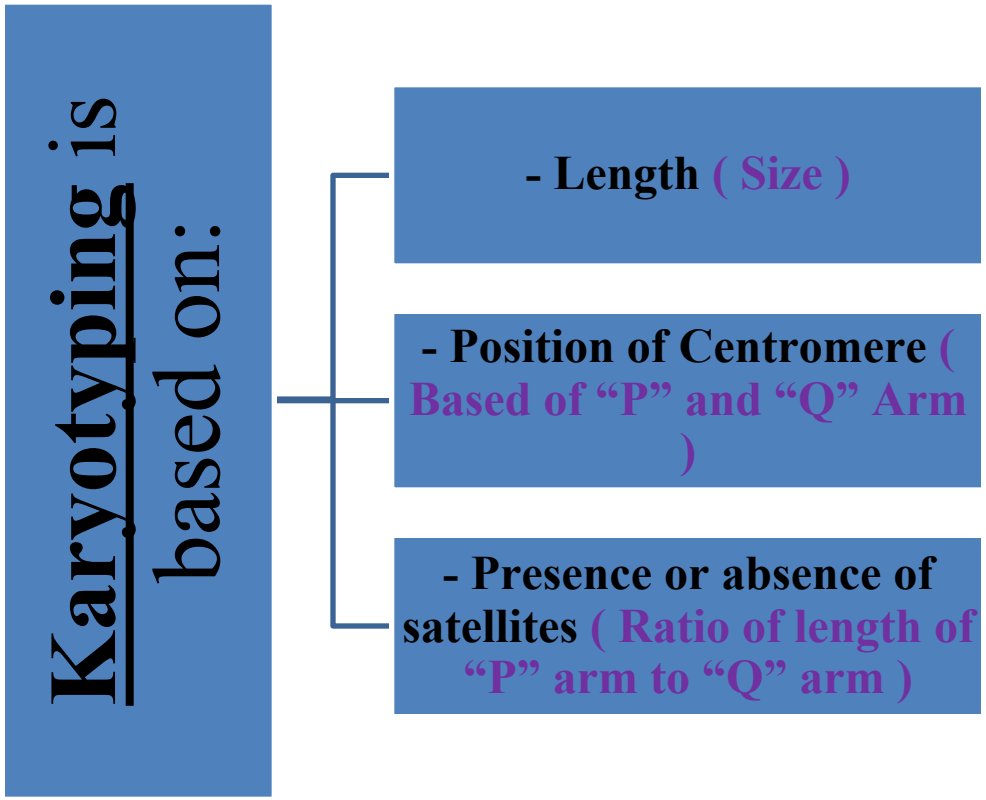
Karyotype :a test looks at the size, shape, and number of your chromosomes.

Steps involved:-

- **Culturing** — the propagation of microorganisms or of living tissue cells in special media conducive to their growth.
- **Harvesting** — To obtain cells, tissues, or organs for grafting or transplantation, from either a donor or the patient.
- **Slide-Making**
- **Banding**
- **Staining**
- **Karyotyping** — In the next slide
- **Chromosome Analysis**



KARYOTYPING



Note: "P" ARM is shorter than the "Q" ARM.

the "Q" ARM could never be shorter than the "P" ARM. (They may be equal in *length*).

ITEMS IN THE DESCRIPTION OF KARYOTYPE:

- **Normal Karyotypes:**

46, XY **(Male)**
46, XX **(Females)**

- **Abnormal Karyotypes:**

47,XY,+ 21	**Down Syndrome**
45,X Or 45,XO	**Turner Syndrome**(loss of X)

Down Syndrome: also called trisomy 21, is a genetic disorder caused by the presence of all or a part of a third copy of chromosome 21.

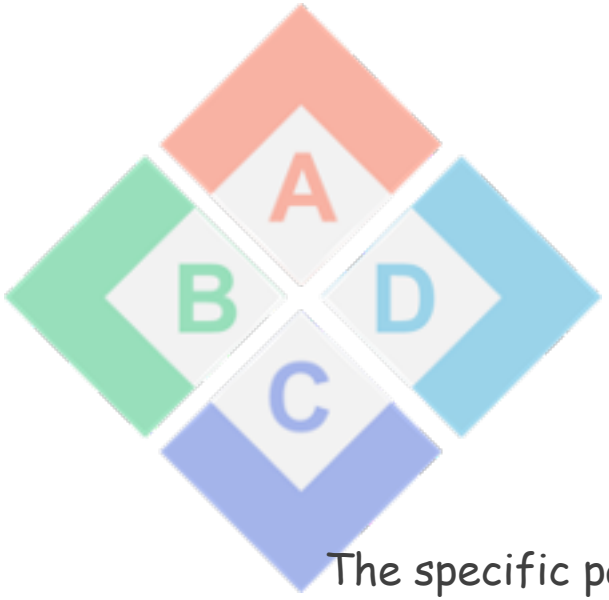
Turner Syndrome: is a genetic condition in which a female is partly or completely missing an X chromosome.

BANDING

Chromosome banding refers to alternating light and dark regions along the length of a chromosome, produced after staining with a dye.

Some staining techniques cause the chromosomes to take on a banded appearance.

Patterns and the nomenclature for defining positional mapping have been standardized.

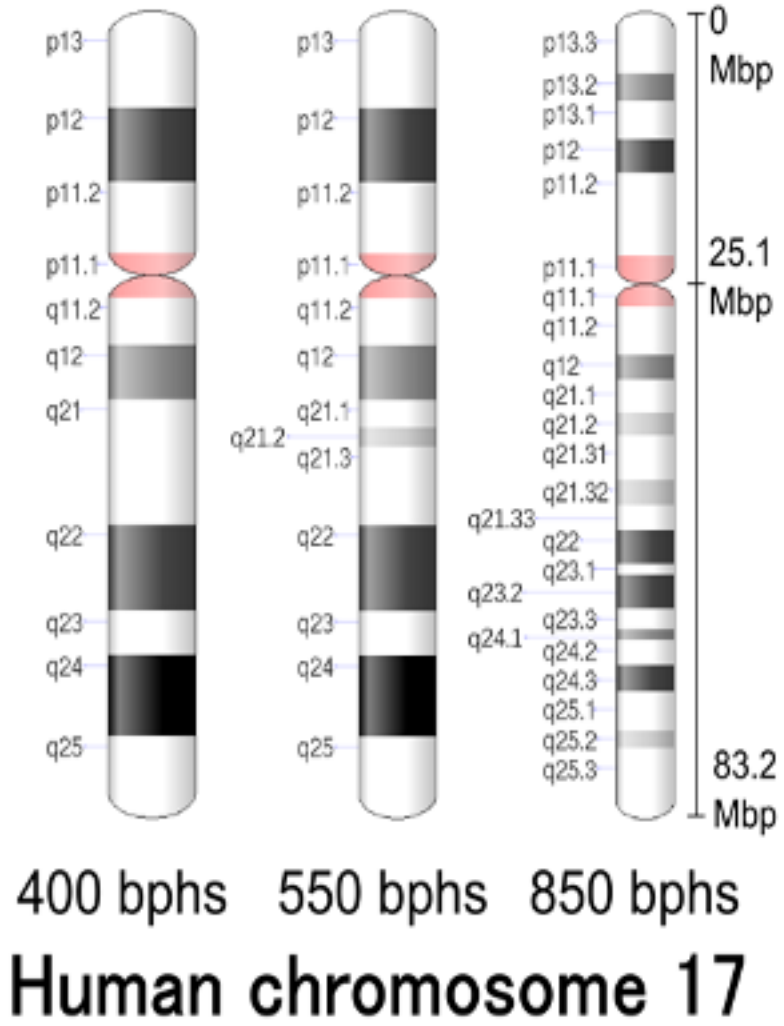


Each arm gets a **specific** and **repeatable** sequence of dark and light bands.

The specific pattern allows for:
- identification of each chromosome
- longitudinal mapping for locating genes
- finding structural changes

CHROMOSOME BANDING

- Band resolution= estimate of number of light + dark bands per haploid set of chromosomes.
- 400 ⟶ 850+



- Disadvantage of low(400 resolution) is inability to detect abnormalities
- As resolution increases detection increases
- light regions are active, Dark regions are inactive

TYPES OF BANDING :

G banding

Treat with trypsin then Geimsa Stain.

R banding

Heat then treat with **Geimsa** Stain.

Q banding

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

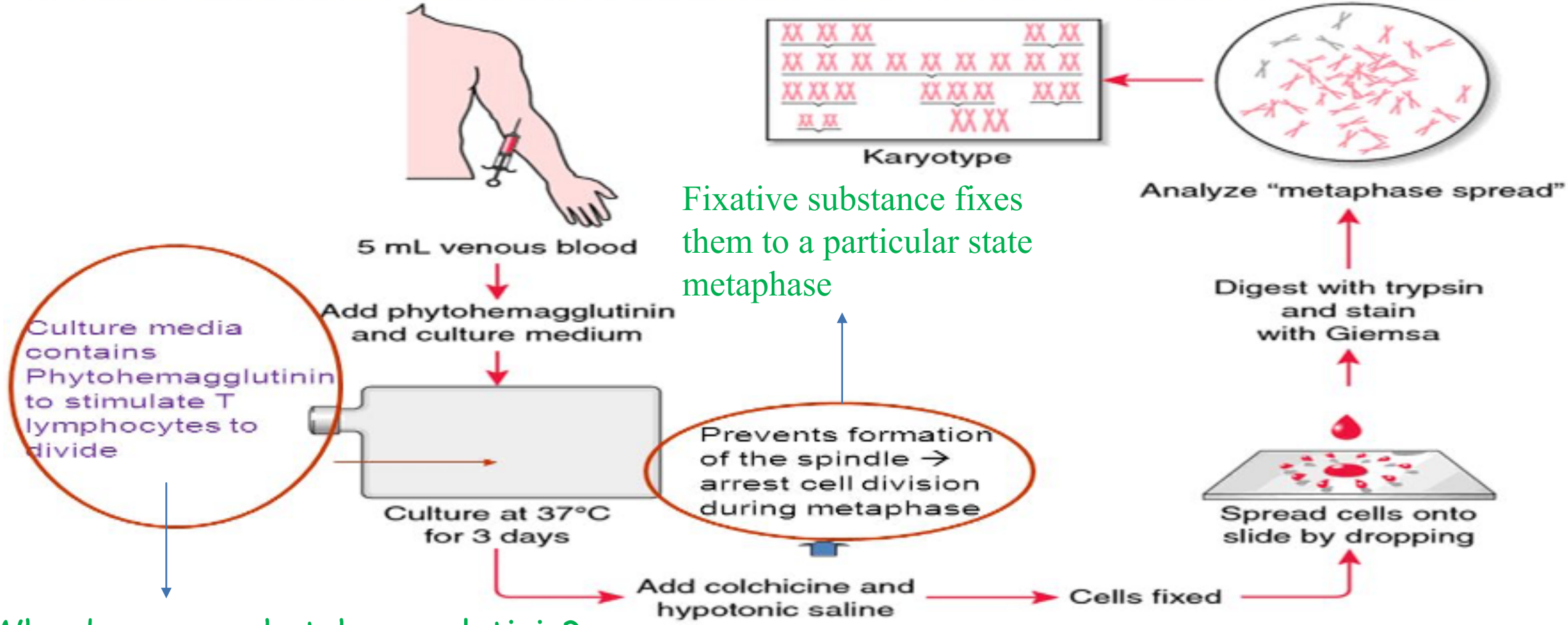
Like G but with different dye (stain)

C banding

Staining of the Centromere. Treat with acid then alkali prior to G banding.

To classify the chromosomes by the centromeres

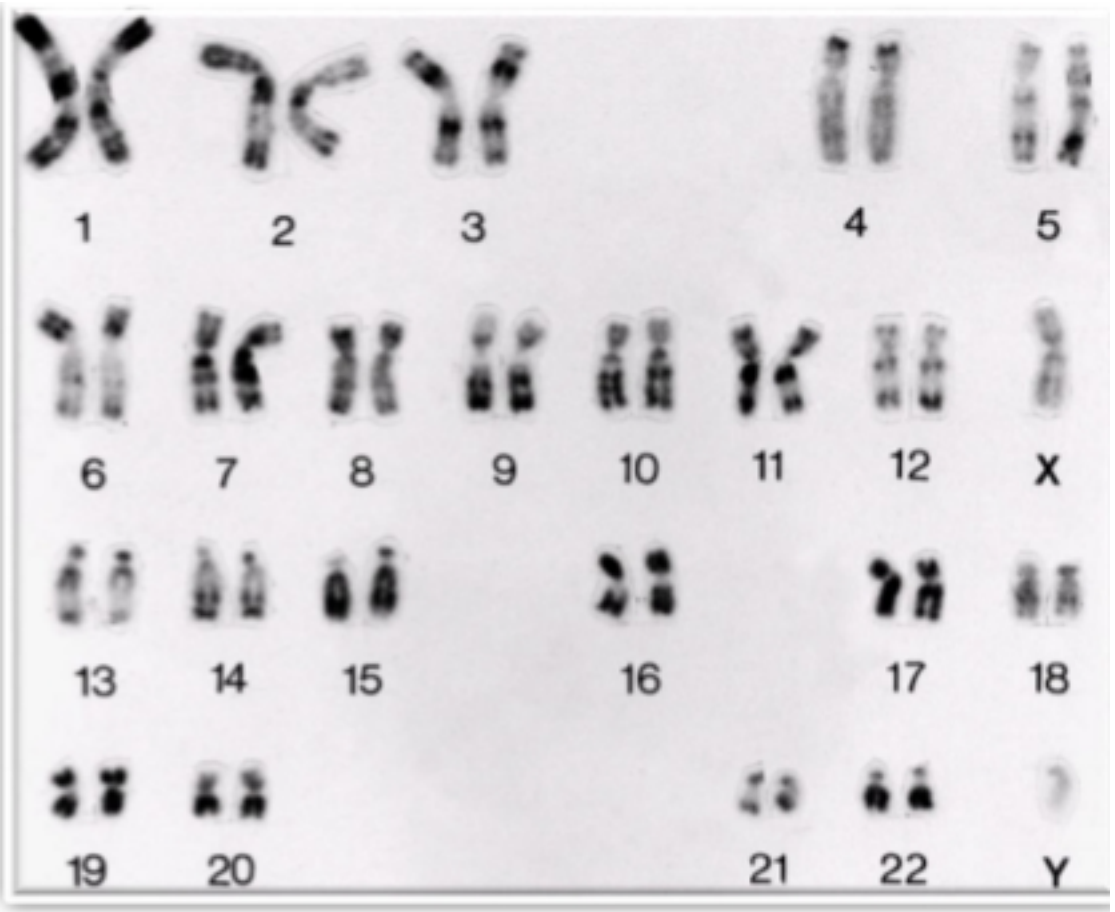
CHROMOSOME PREPARATION FROM PERIPHERAL BLOOD



Fixative substance fixes them to a particular state metaphase

Why do we use phytohemagglutinin?
We use it to increase their(cells) number by increasing the rate of division

A normal G-banded male Karyotype

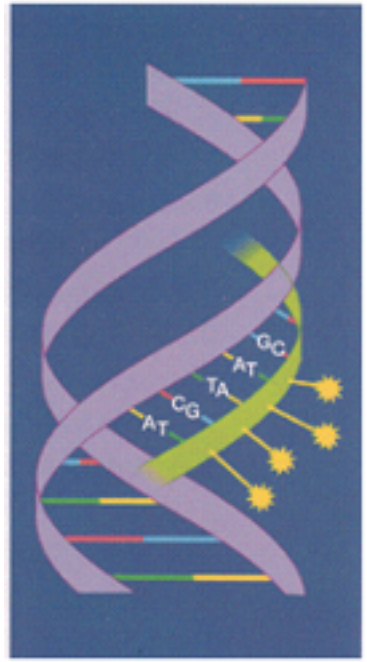


A normal R-banded male Karyotype

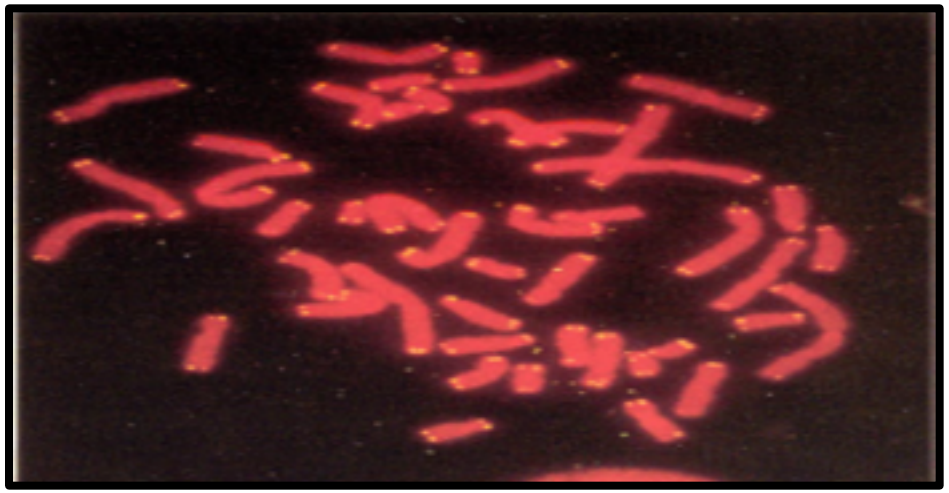
(F.I.S.H🐟) FLUORESCENCE IN SITU HYBRIDIZATION

in-situ= in its place , determines the chromosomes and its position Extremely accurate detection happens at the intermolecular level: **finding the centromere** of a chromosome.

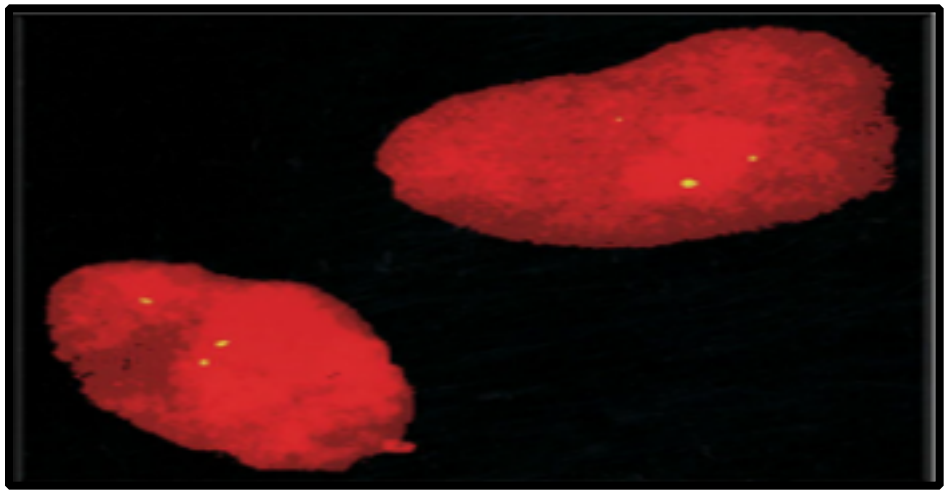
- **F.I.S.H** can be used in both **metaphase** and **interphase**.
- **Karyotyping** can only be used for **metaphase**.



F.I.S.H🐟) FLUORESCENCE IN SITU HYBRIDIZATION



- 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.

ببساطة :هذه التقنية تُستخدم لتحديد و إظهار بروتينات أو مواد جينية أخرى، و لكنّها محدودة لإظهار جزء مرغوب معيّن، و هذه من السلبيات حيث لا نستطيع اكتشاف مرض محدد إلا بعد استخدام التقنية المحددة لهذا المرض أو هذا الجزء المرغوب.

كيف؟ هذه العملية السريعة نسبياً و تكون عن طريق دمج أعواد مضيئة مصنّفة، مع شريط واحد من الدي إن إي مثلاً؛ لتحديد :مناطق معيّنة أو مناطق حذف أو تبديل)سيتم شرح هذه المناطق في المحاضرة القادمة(437*

TAKE HOME MESSAGES

- The packaging of DNA into chromosomes involves several orders of DNA coiling and folding.
- The normal human karyotype is made up of 46 chromosomes consisting of 22 pairs of autosomes and a pair of sex chromosomes, XX in the female, and XY in the male.
- Each chromosome consists of a short (p) and a long (q) arm joined at the centromere.
- Chromosomes are analyzed using cultured cells and specific banding patterns can be identified using special staining techniques.
- FISH is based on the ability of a single-stranded DNA probe to anneal to its complementary target sequence. It can be used to identify and study genes on chromosomes in metaphase or interphase.

MCQs

Q1:**It's used to to stimulate T lymphocytes to divide**

D) Phytohemaggluti nin (PHA)	C) Geimsa Stain	B) trypsin	A) Colchicine

Q2:…… is based on the ability of a single-stranded DNA probe to anneal to its complementary target sequence. It can be used to identify and study genes on chromosomes in metaphase or interphase :

D) Quinidine	C) FISH	B) Banding	A) Karotype

Q3:The 2 sister-chromatids held together at:

D) Isoelectric region	C) Centromeric region	B) Stop region	A) Promoter region

Q4: …… is used to arrest cell division during metaphase for karyotyping

D) Phytohemagglutinin (PHA)	C) Trypsin	B) C Banding	A) Colchicine

MCQs answers

4) A
3) C
2) C
1) D

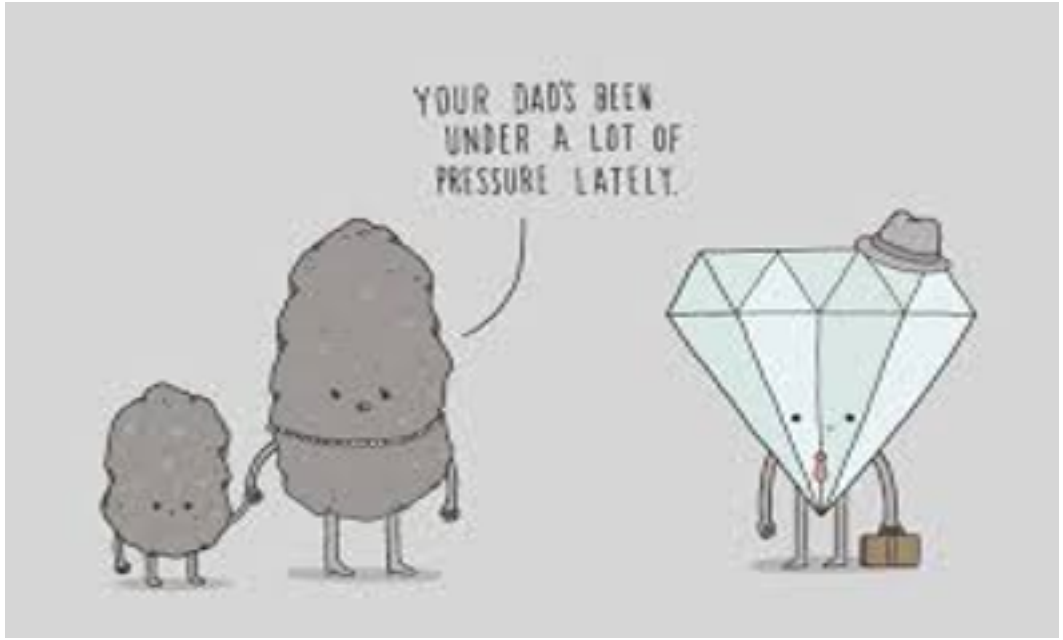
MCQs

Q5: **The end of each chromosome is**

D) FICH	C) telomere	B)colchicine	A) PROPHASE

Q6:**The genotype 47,XY,+ 21 is for …….. Syndrome**

D) Apert syndrome	C) Normal	B) Turner Syndrome	A) Down Syndrome



MCQs answers

6) A

5) C

Boys team:

- Nawaf Alghamdi
- Ahmed Alkhawashki
- Bassam Alasmari
- Rayan Alzahrani
- Khalid AlOsaimii
- Abdulrahman Alswat
- Faisal AlFadel
- Hadi AlHemsi
- Hesham Alsqabi
- Yazeed Alomar
- Mohammed Benhjji
- Badr Alshahrani
- Homoud Algadheb

Girls team:

- Ghaida Alasiri
- Arwa Alqahtani
- Albandri Ahmad
- Aljohara Albnyan
- Aljohara alshathry
- Alanoud Alshahrani
- Raghad Alasiri
- Renad Alhmidi
- Sara Alharbi
- Taif Almutari
- Abeer Awad
- Ghada Alabdi
- Noura Almassad
- Hind Almut

Team Leaders:

- Sumo Abdulrahman
- Abdulmalik Mokhtar

: HumanGenetics439@gmail.com

Editing File

Human Genetics 439