

GENETICS

LECTURE 1 AND 2

Katarzyna Osmańska-Załuska, PhD



CONTACT:

k.osmanska-zaluska@powislanska.edu.pl

or

Microsoft Teams Chat

ABOUT THE COURSE

- Nursing – 1st degree (bachelor's), 1st year
 - 8 lectures, 3 hours each (24 hours altogether)
 - Written exam with mark
 - Multiplechoice test
 - 50 questions, 4 answers, 1 answer correct
 - Time: 60 minutes
 - Correct answer – 2 point
 - Wrong answer – 0 point

TEST EVALUATION CRITERIA

Assessment	Very good (5.0)	Good plus (4.5)	Good (4.0)	Sufficient plus (3.5)	Sufficient (3.0)	Insufficient (2.0)
% of correct answers	93-100%	85-92%	77-84%	69-76%	60-68%	59% and less
Number of points scored	93-100	85-92	77-84	69-76	60-68	59 and less

$$\begin{aligned} &\text{Number of points scored} \\ &= \\ &\quad \text{Number of points scored during ending test} \\ &+ \\ &\quad \text{Number of points scored during tests after lectures} \end{aligned}$$

NUMBER OF POINTS SCORED DURING TESTS AFTER LECTURES

○ Extra points

- Multiplechoice test at the end of each lecture – 4 answers, 1 answer correct
- Tests just for volunteers → Microsoft Teams → Assignments
- The test occurs at particular time – 15 minutes before the end of the lecture
- First 3 students with all good answers will get 3 points
- Each student with all good answers will get 1 point
- After all lectures are sum up and added to points from ending test

○ Examples:

- Student A gets:
 - 85 points from ending test (mark 4.5)
and
 - 8 points from tests after lectures
altogether 93 points – mark 5.0 (better mark 😊)
- Student B gets:
 - 58 points from ending test (mark 2.0 – failed 😞)
and
 - 5 points from tests after lectures (points are added whether the test is passed or not)
altogether 63 points – mark 3.0 (pass 😊)

BUNA – INDEPENDENT STUDENT WORK

- An essay; 2-3 pages A4, font: New Times Roman, 12
- The list of topics of essays: General -> Files -> Class Materials (list will be available during this weekend)
- Bibliography
- Name, surname and field of study
- Send to my email k.osmanska-zaluska@powislanska.edu.pl
- Deadline: 12th January 2023

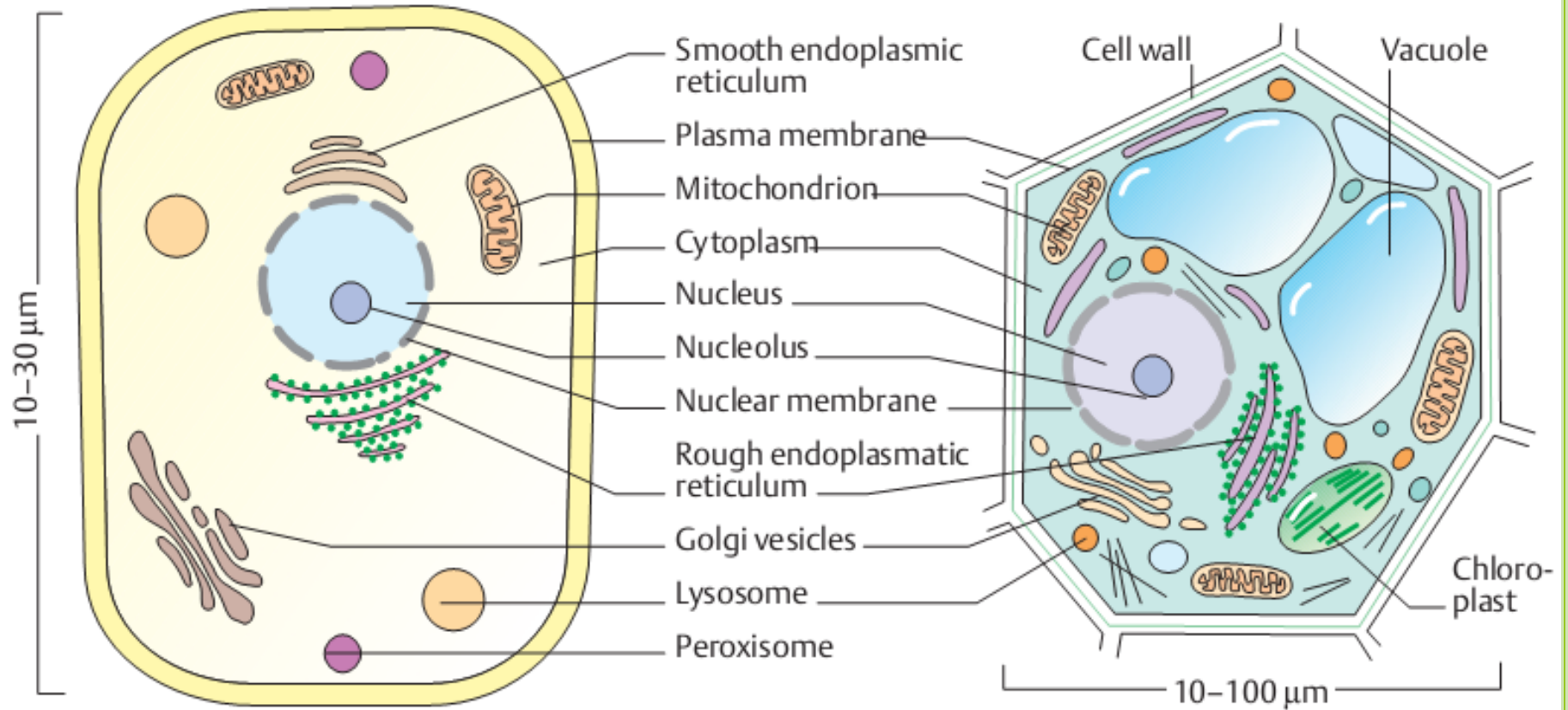
LITERATURE:

1. Tobias E.S., Connor M., Ferguson - Smith M.: Medical Genetics. 6th Edition. Wiley-Blackwell 2011.
2. Jorde L.B., Carey J.C., Bamshad M.J.: Medical Genetics. 6th Edition. Elsevier 2019.
3. Friedman J.M., Dill F.J., Hayden M.R., McGillivray B.C.: Genetics (National Medical Series for Independent Study). 2nd Edition. Lippincott Williams and Wilkins 1996

WHAT ARE WE GOING TO DO TODAY?

1. Cell cycle
2. Mitosis, meiosis
3. Definitions: karyotype, karyogram
4. Chromosomal aberrations
5. Indications for performing chromosome analysis





1. Animal cell

2. Plant cell

B. Scheme of an eukaryotic cell

CELL CYCLE

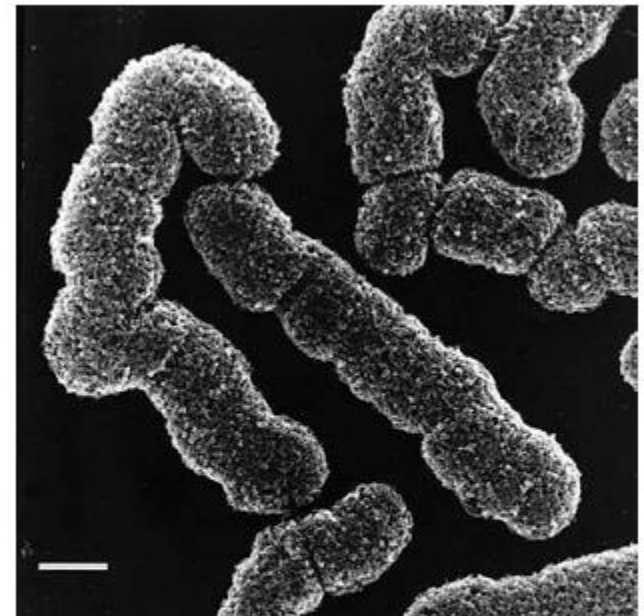
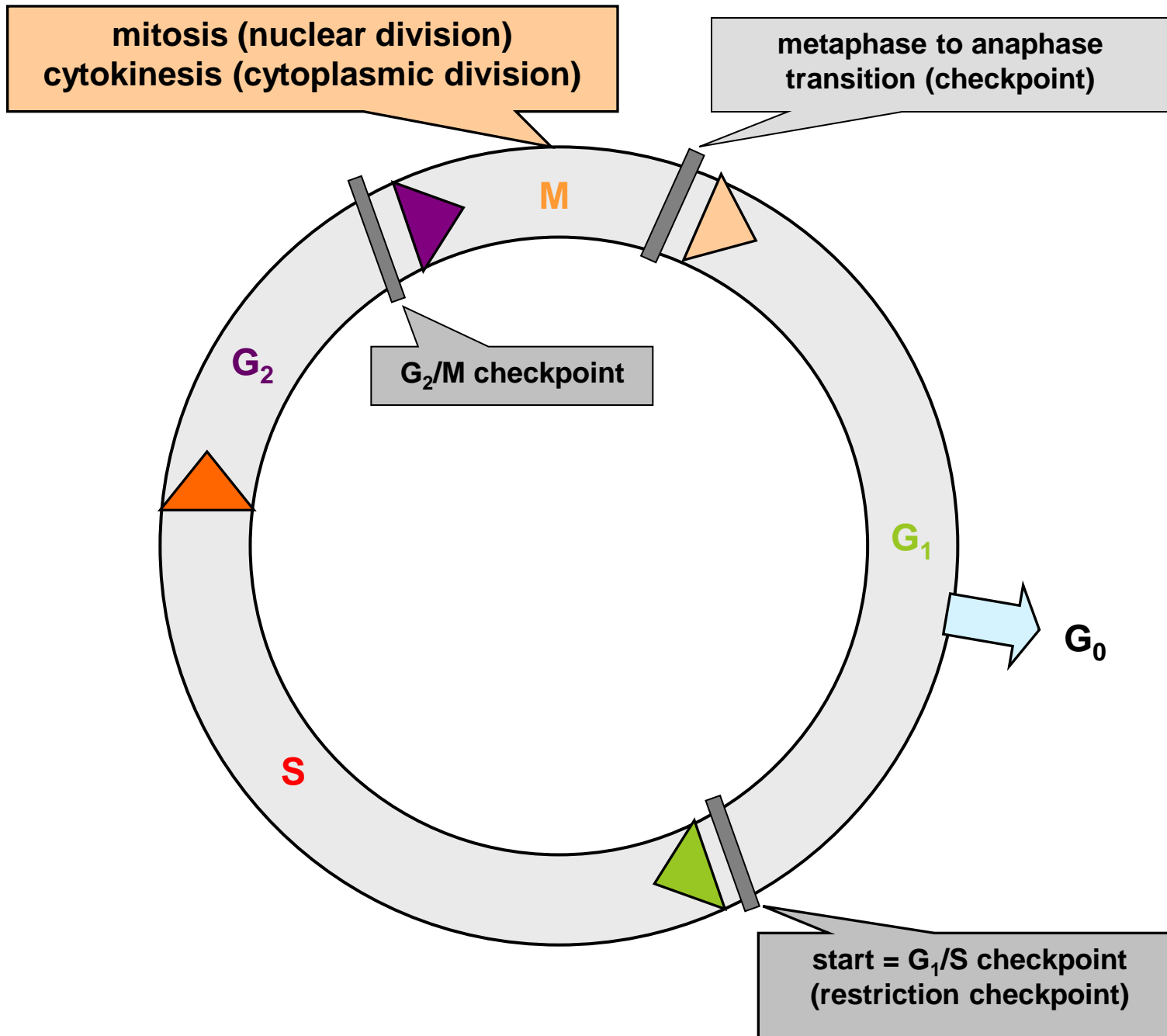
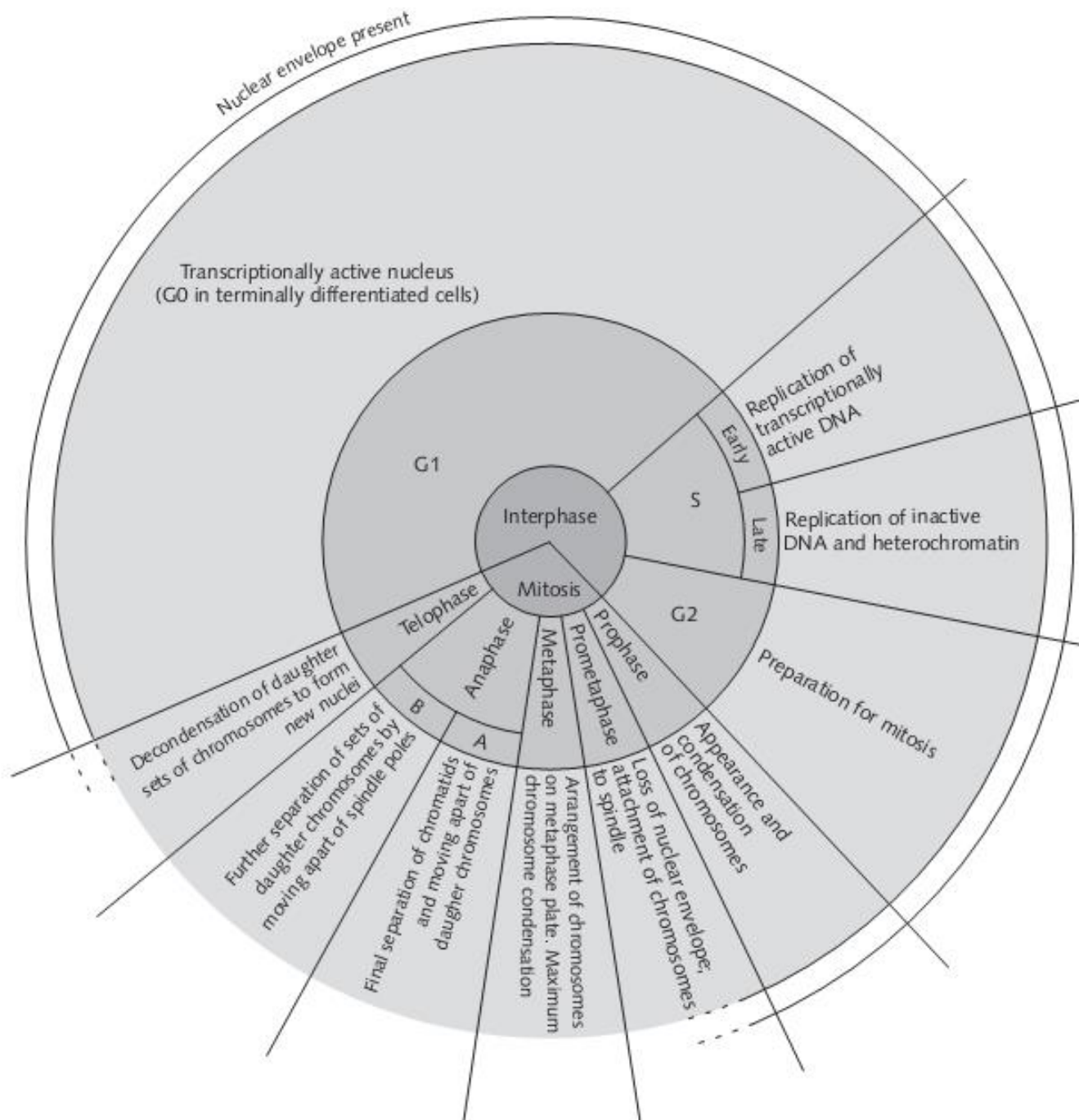


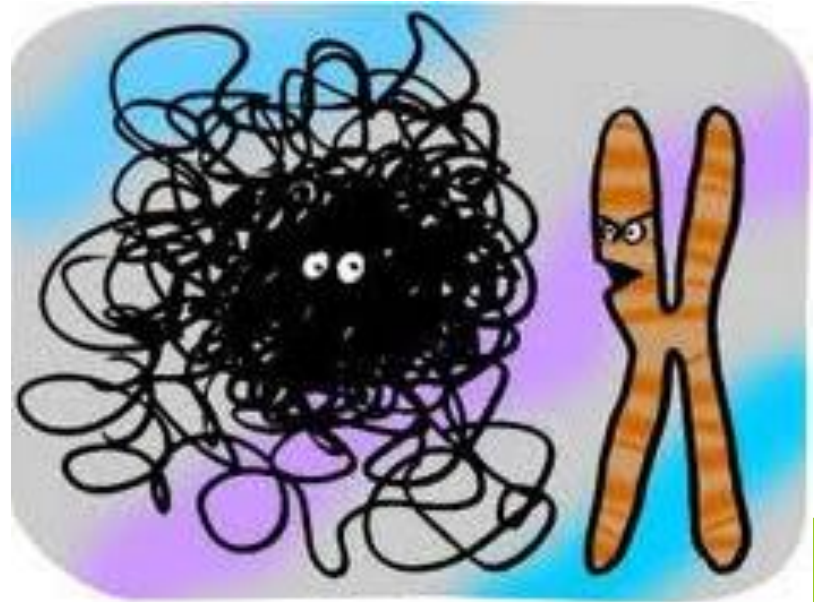
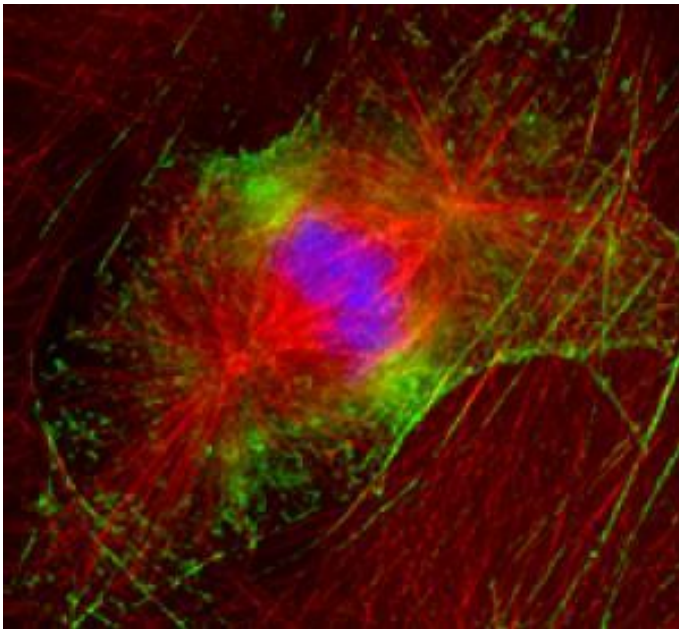
Figure 2.4 Scanning electron micrograph of an early prophase chromosome, showing that it is not yet split into two separate chromatids. Scale bar = $2\mu\text{m}$. Reproduced with permission from Sumner (1991) *Chromosoma* **100**, 410–418, © Springer-Verlag.







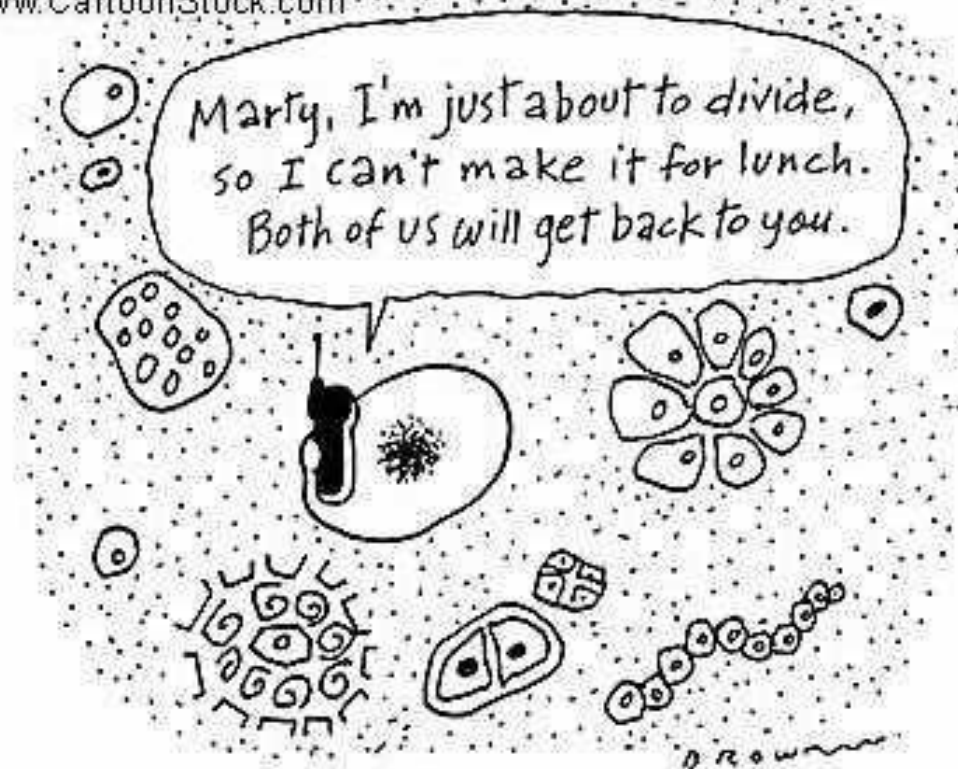
CELL DIVISIONS



Dude, mitosis starts in five minutes...
I can't believe you're not condensed yet.

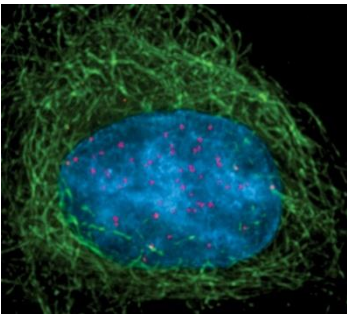
MITOSIS

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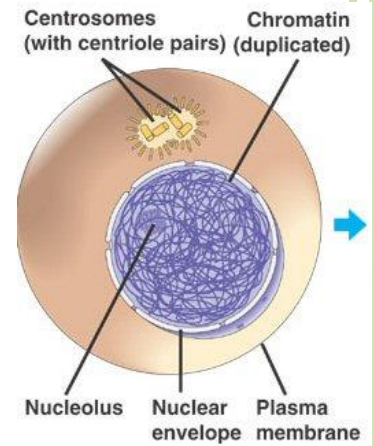


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THE CELLULAR PHONE

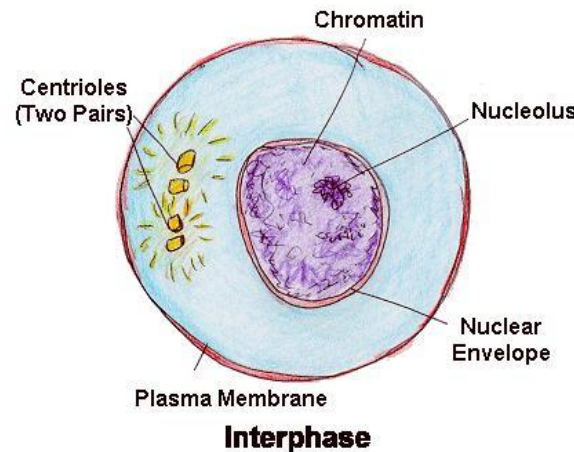


INTERPHASE



- Period between successive mitoses and it consists of three phases:

- G1 – 6-12 h,
- S – 6-8 h,
- G2 – 3-4 h

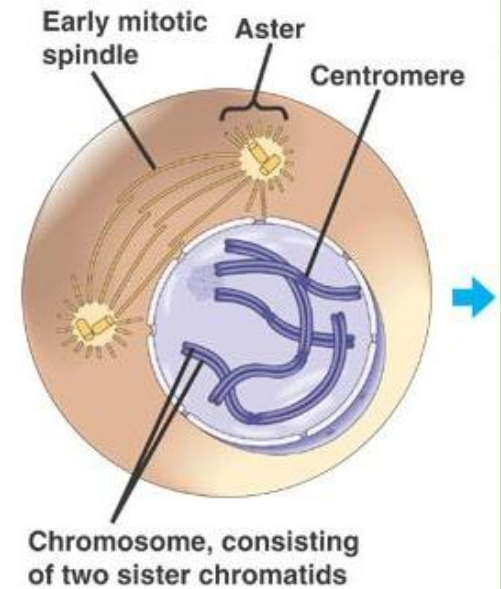


- Thin chromatin strands commonly appear as amorphous granular material in the nucleus of stained cells.

M-PHASE (MITOSIS)

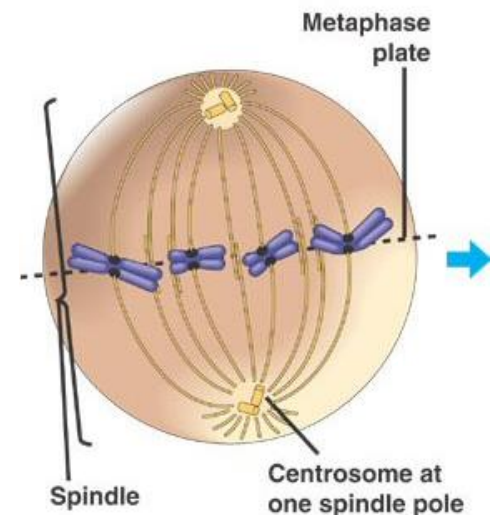
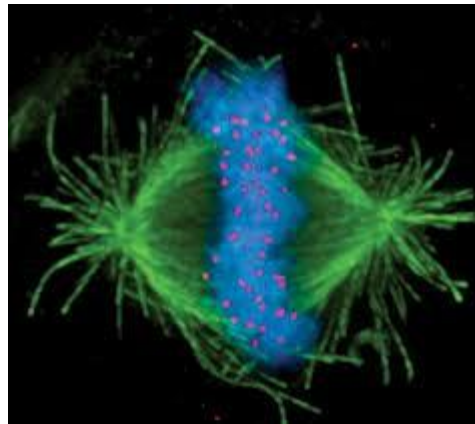
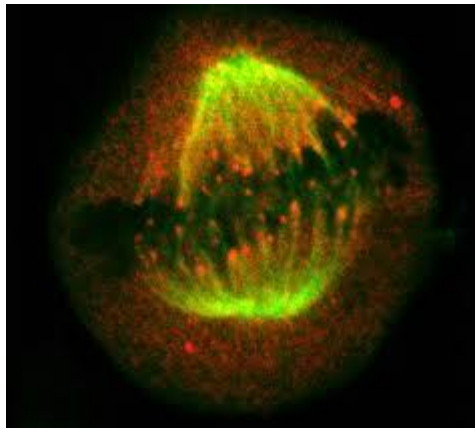
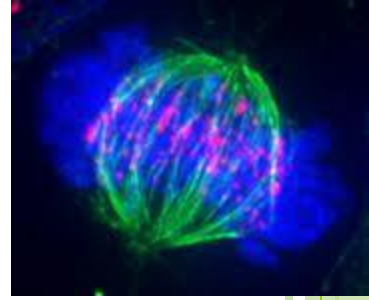
A) PROPHASE:

- Chromosomes condense,
- Two chromatids are connected at their centromeres



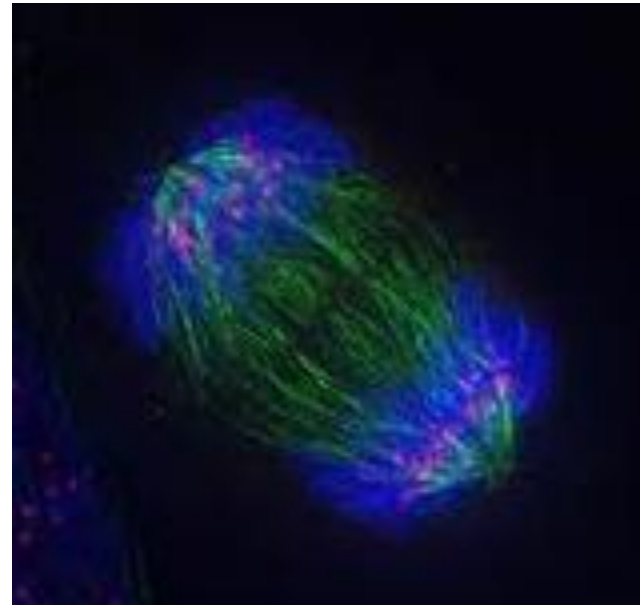
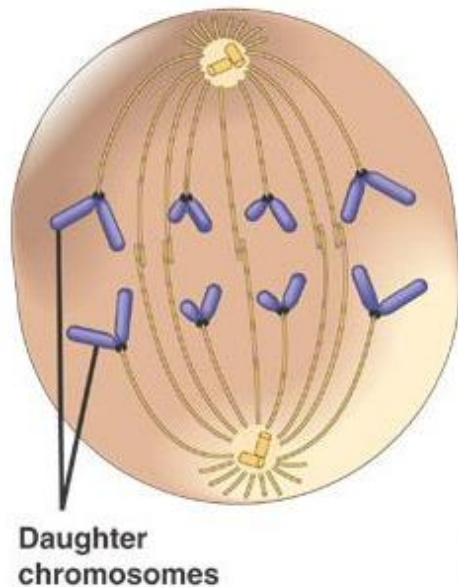
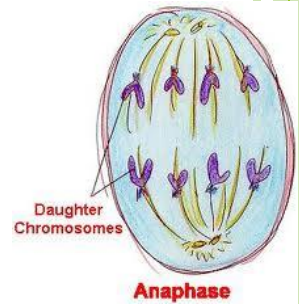
B) METAPHASE:

- Kinetochore fibres from opposite microtubule organising center (MTOC) push and pull on the joined centromeres of sister chromatids causing each chromosome to move,
- The position in the center of the cell is called **metaphase plate**,
- The chromosomes are kept in this position by the tension from fibers of opposite MTOCs.

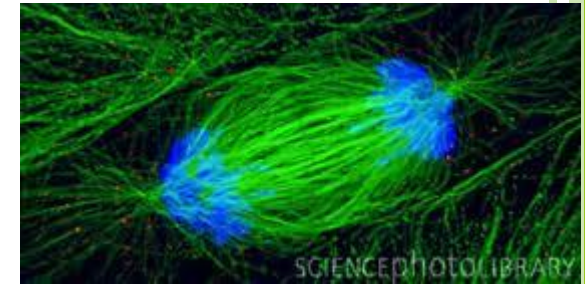


C) ANAPHASE:

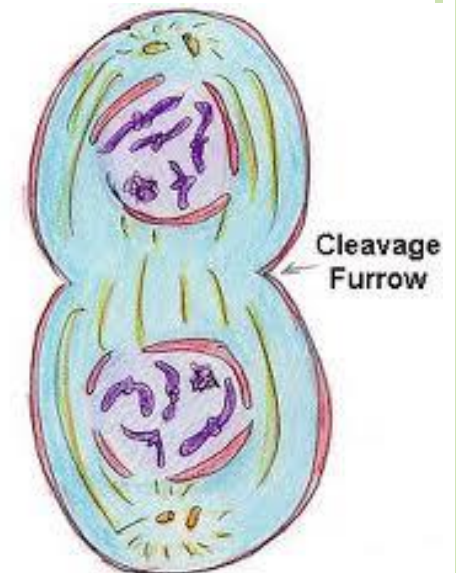
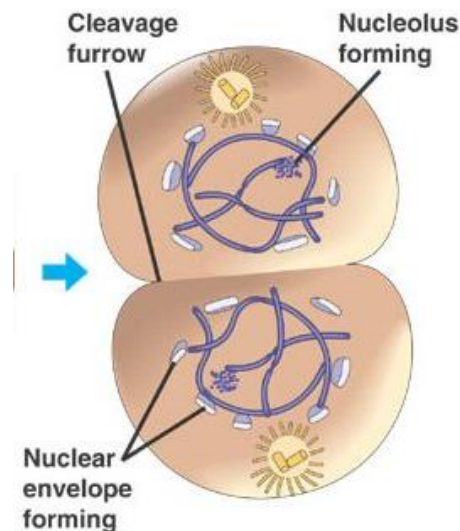
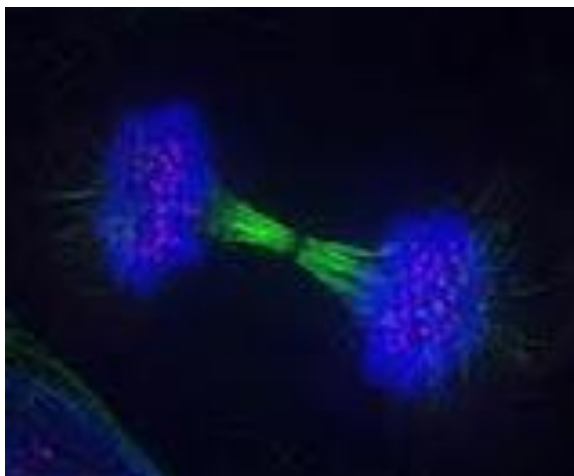
- Sister chromatids separate at the centromere and are pulled to opposite poles of the cell,
- As each chromatid moves through the cytosol, its arms drag along behind its centromere.



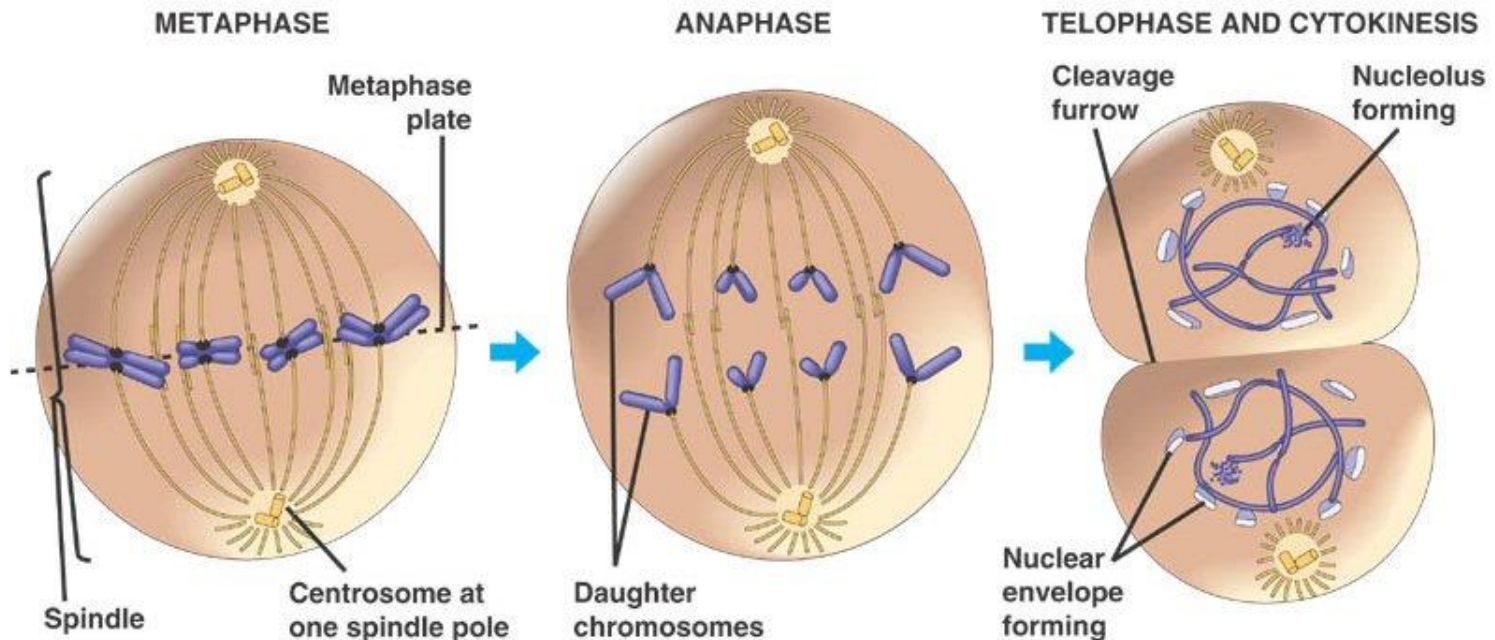
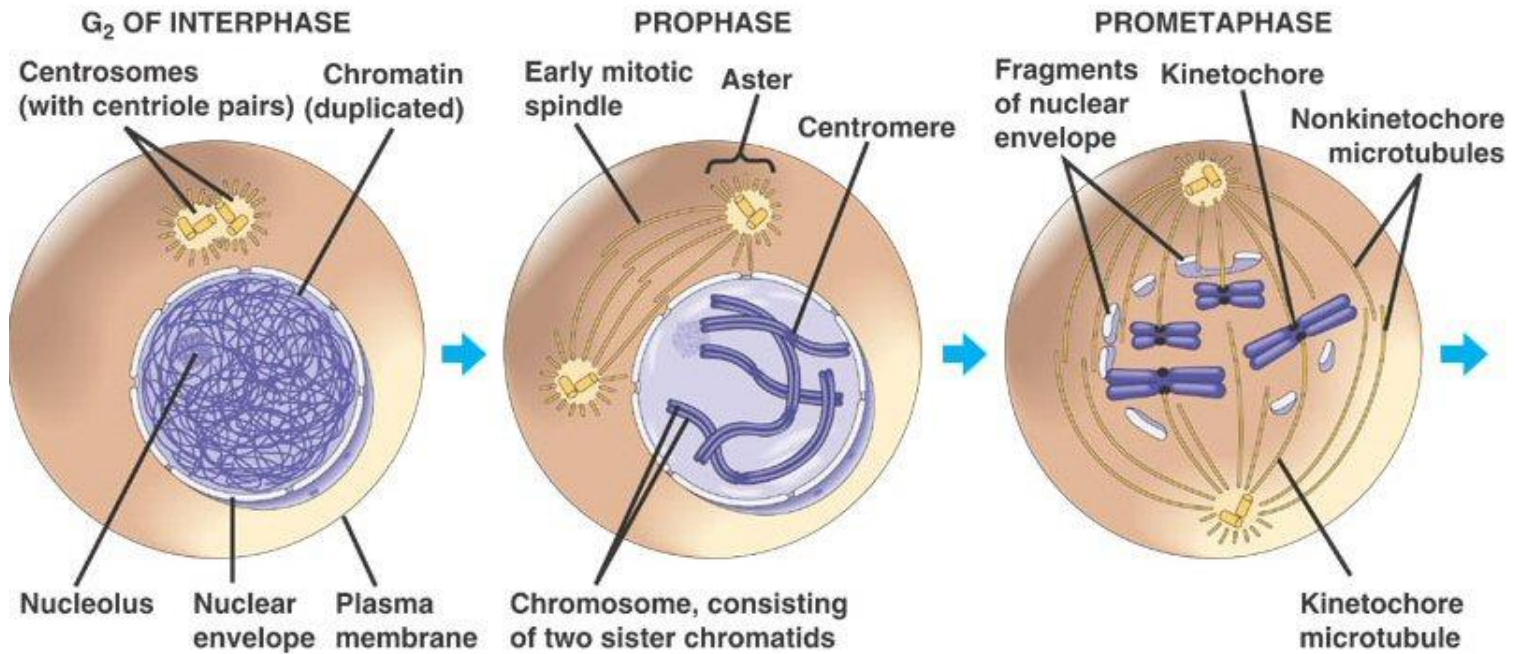
D) TELOPHASE:



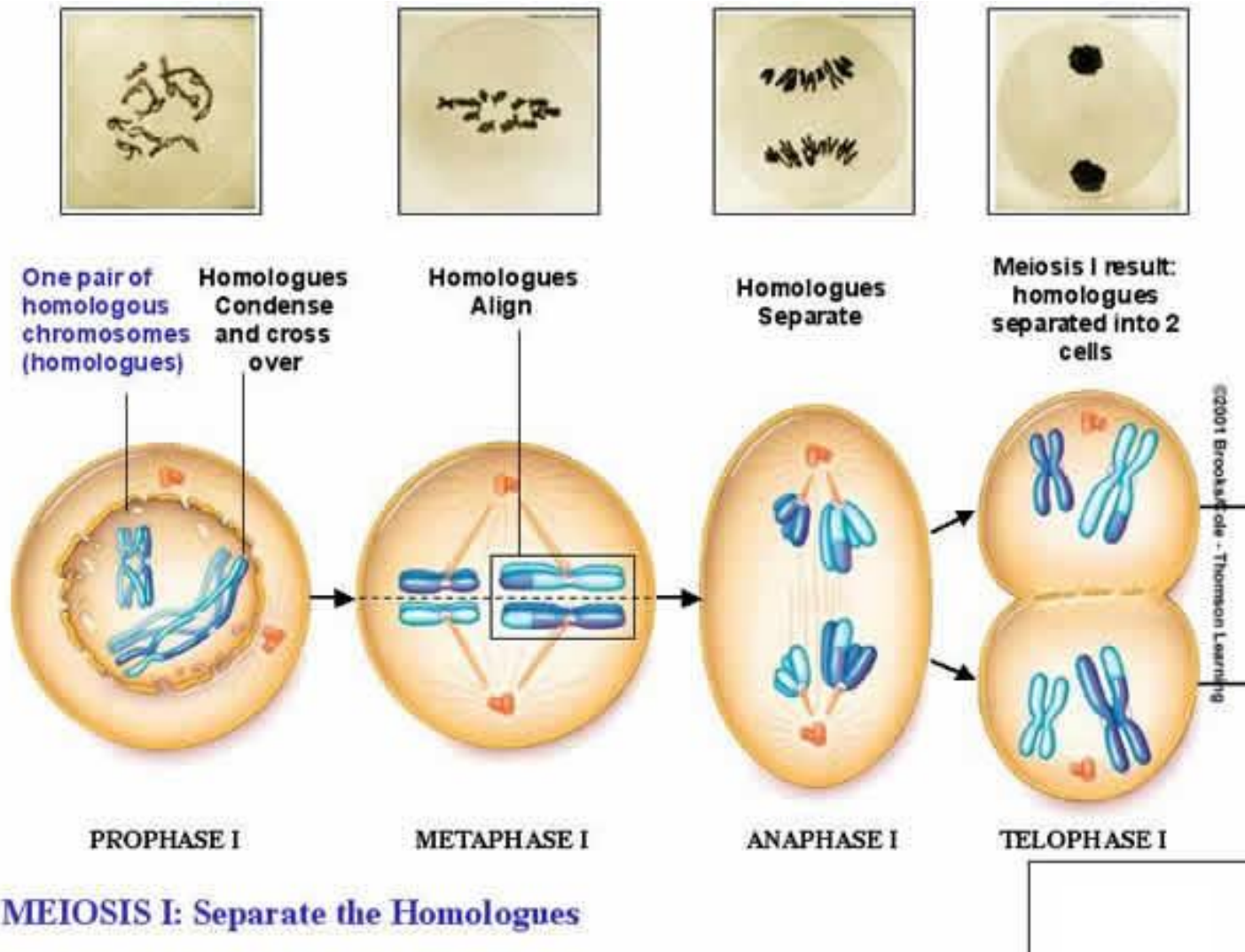
- Each set of separated chromatids is assembled at the two poles of the cell.
- The chromosomes begin to uncoil and return to an interphase condition.
- The spindle degenerates, the nuclear membrane reforms, the cytoplasm divides in a cytokinesis.



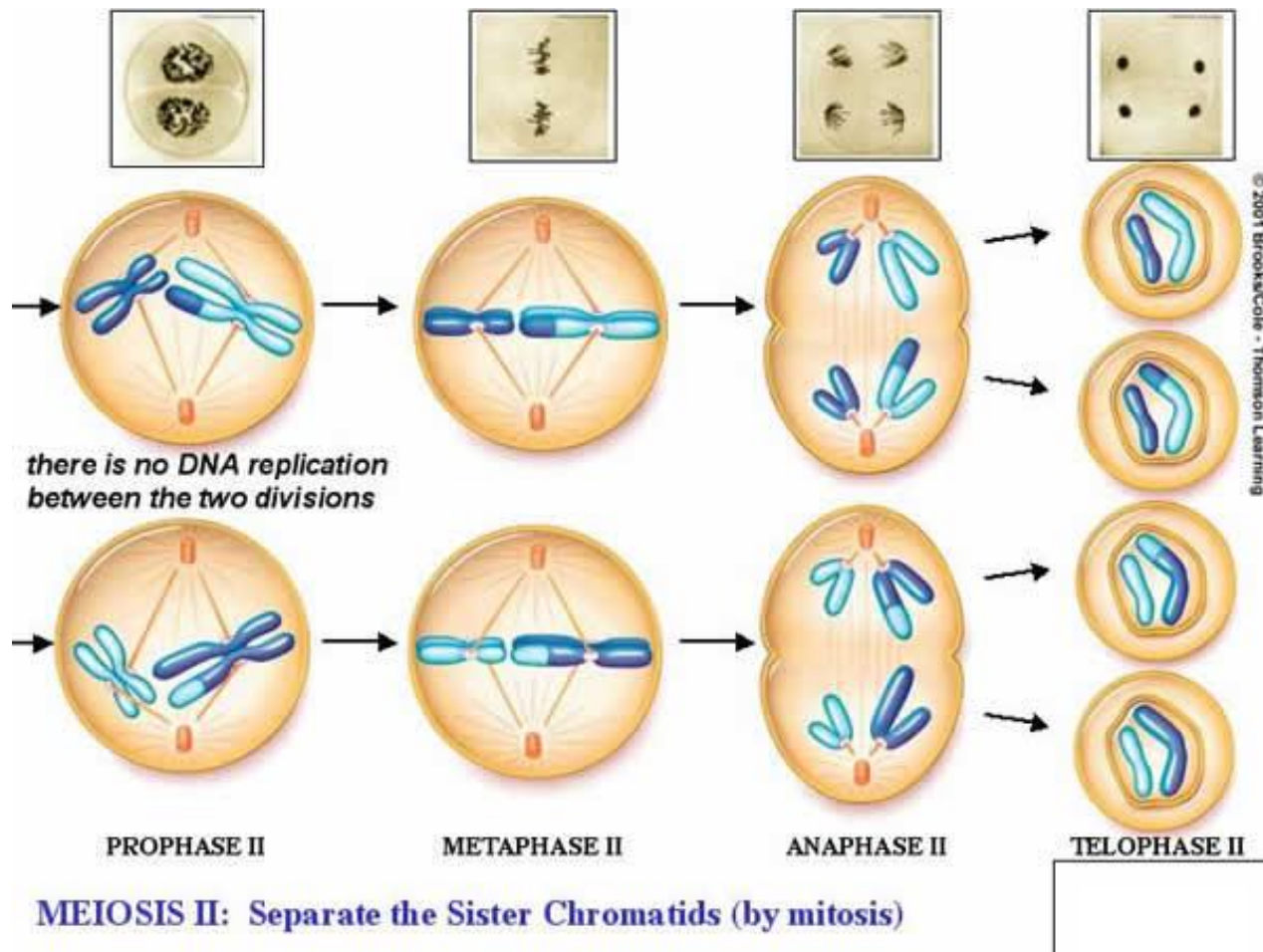
Telophase and Cytokinesis



MEIOSIS I



MEIOSIS II



MITOSIS

An equational division that separates sister chromatids.

One division per cycle.

Homologous chromosomes do not synapse; no chiasmata form.

Genetic exchange between homologous chromosomes does not occur.

Two daughter cells produced per cycle.

MEIOSIS

Meiosis I is a reductional division that separates homologous chromosomes; sister chromatids separate during meiosis II.

Two cytoplasmic divisions: one following reductional chromosomal division meiosis I and one following equational chromosomal division meiosis II.

Chromosomes synapse and form chiasmata.

Genetic exchange occurs between homologous chromosomes.

Four daughter cells produced (gametes).

MITOSIS

Genetic content of mitotic daughter cells is identical to mother cell.

Chromosome number of daughter cells is the same as that of the mother cell.

Mitotic products are usually capable of undergoing additional mitotic divisions.

Normally occurs in almost all somatic cells through the life of the organism.

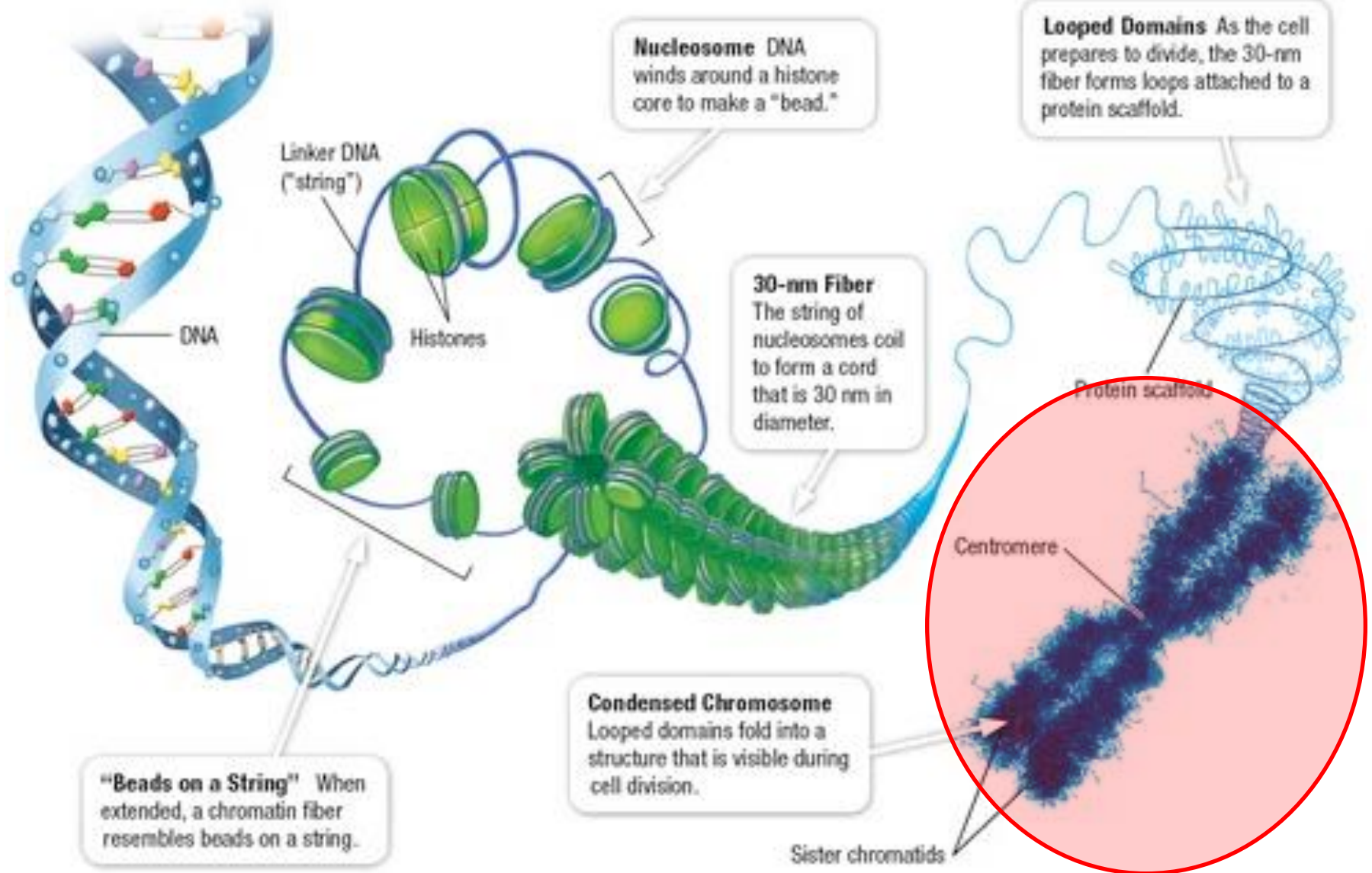
MEIOSIS

Genetic content of meiotic daughter cells is different from each other and from the mother cell.

Meiotic products cannot undergo additional meiotic divisions, although they may undergo subsequent mitotic divisions.

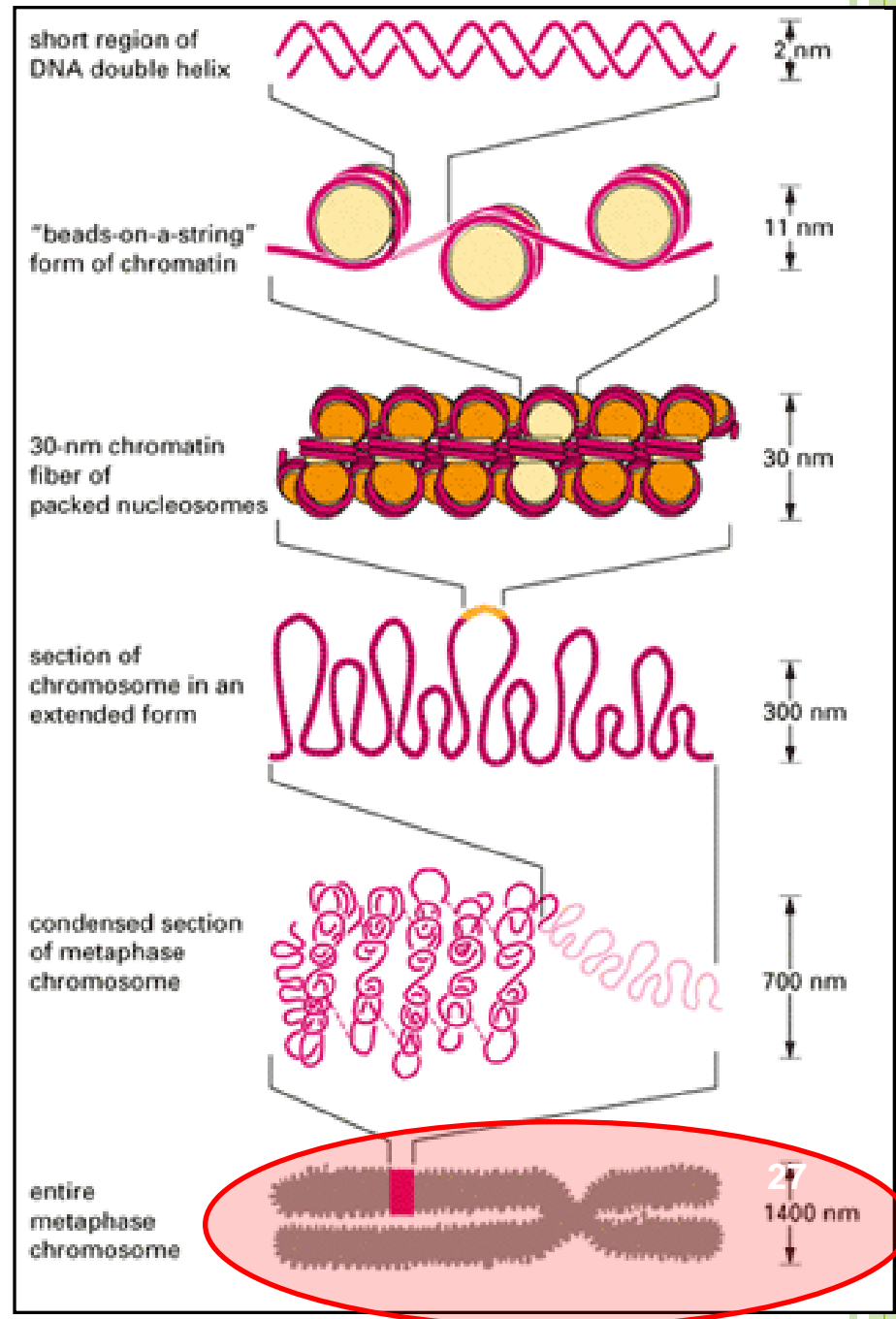
Occurs only in specialised cells of the germ line in the mature organism.

Eukaryotic Chromosome Structure

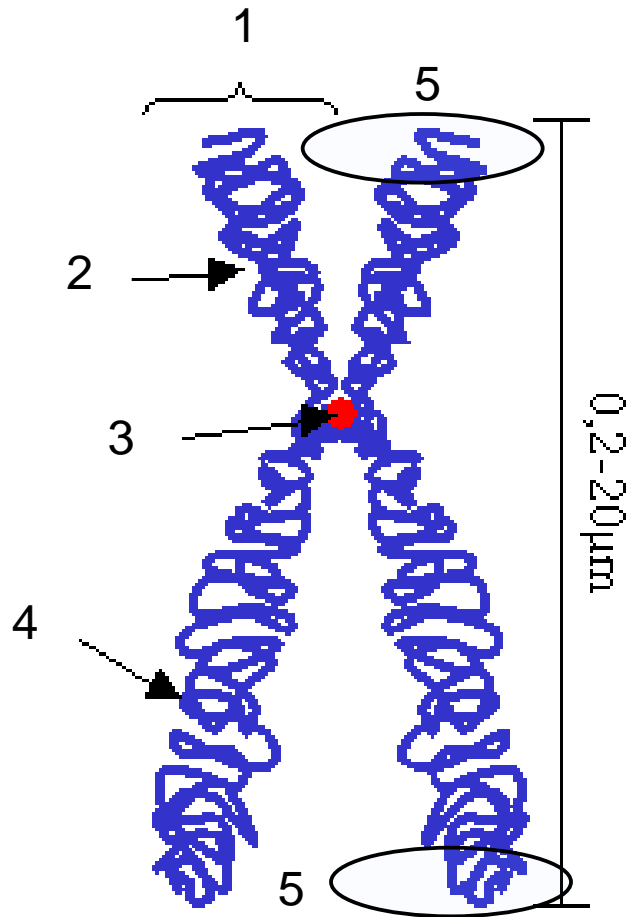


Chromosome

- (gr.) chromo (staining) + soma (body)
- organized structure of DNA and proteins

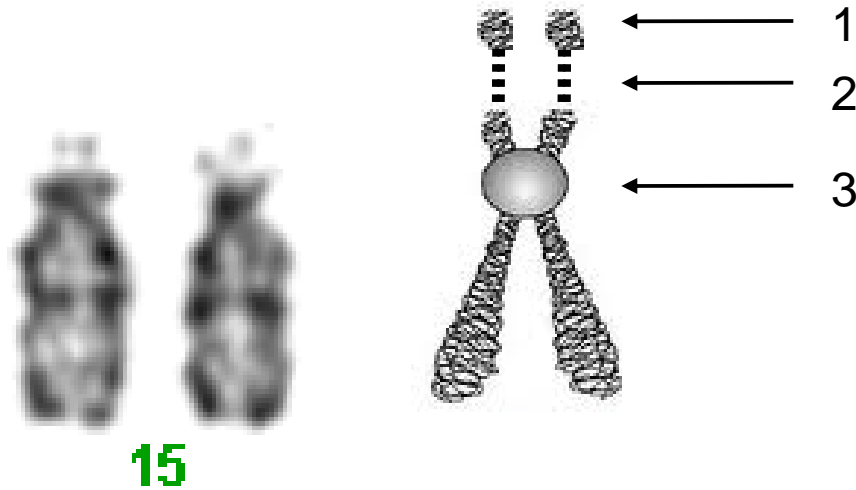


MORPHOLOGY OF CHROMOSOME



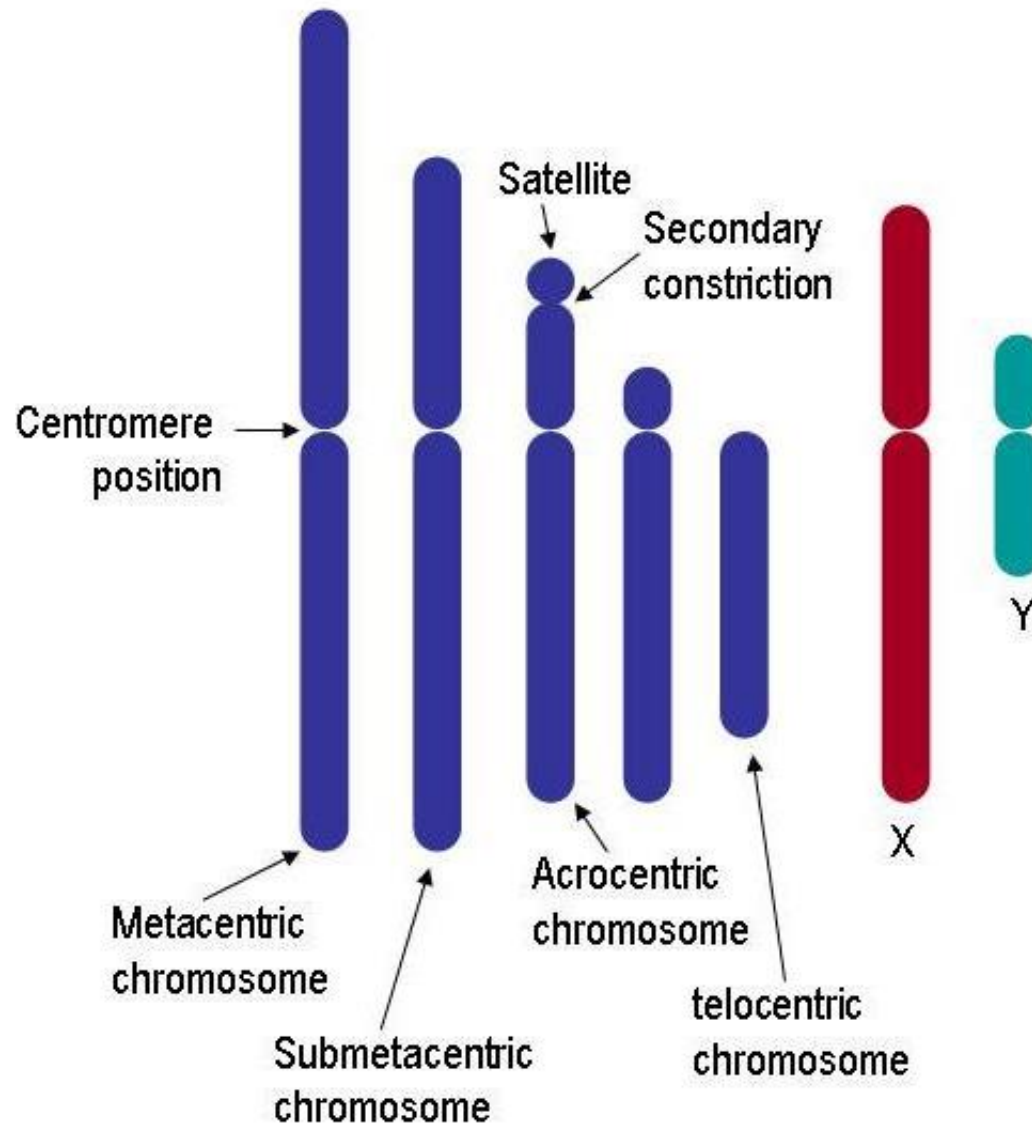
- 1. CHROMATID
- 2. SHORT ARM (p)
- 3. CENTROMERE
- 4. LONG ARM (q)
- 5. TELOMERE

MORPHOLOGY OF CHROMOSOME



- 1. SATELLITES
- 2. NOR (Nuclear Organizer Region)
- 3. CENTROMERE

MORPHOLOGY OF CHROMOSOME



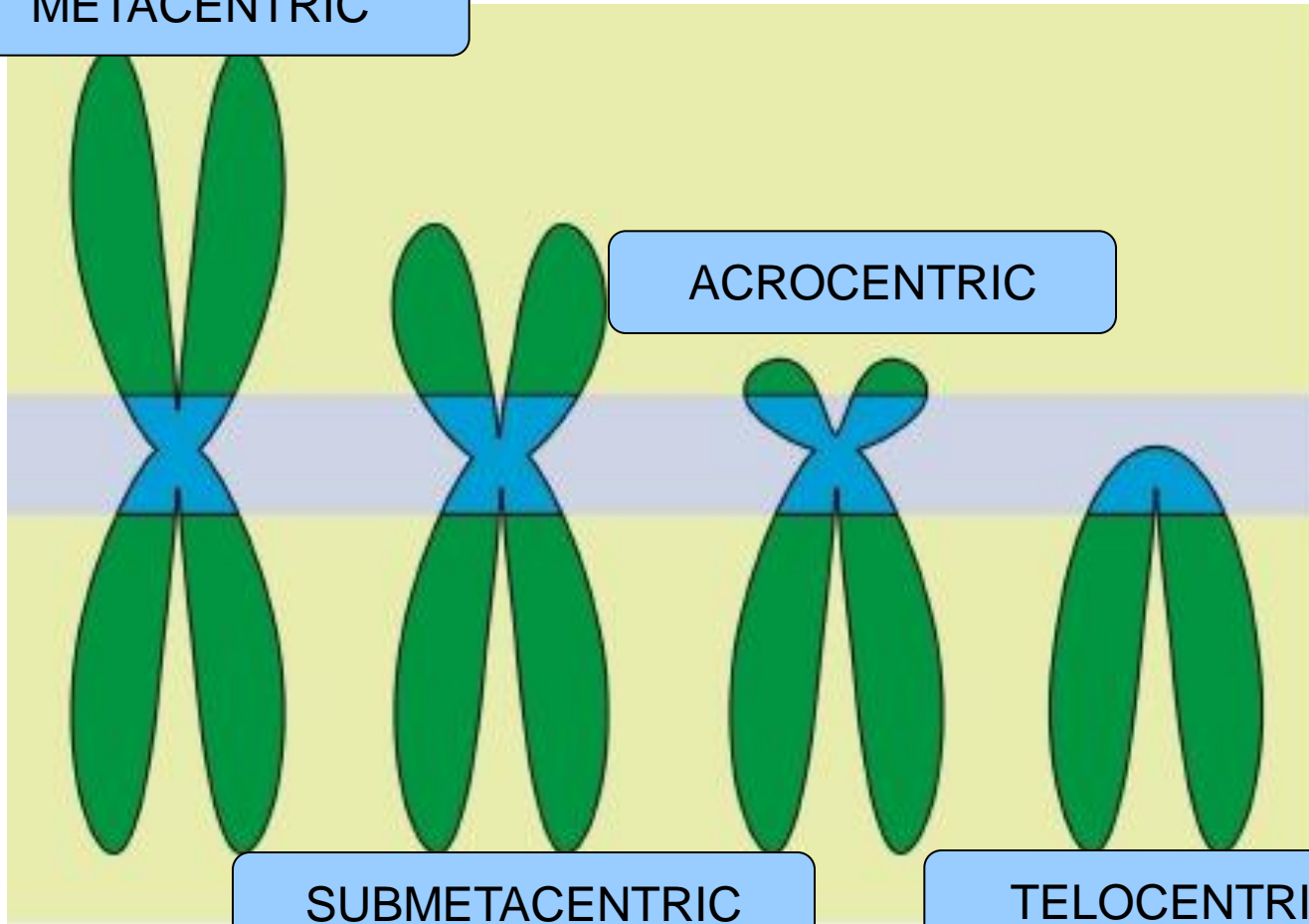
MORPHOLOGY OF CHROMOSOME

METACENTRIC

ACROCENTRIC

SUBMETACENTRIC

TELOCENTRIC



MORPHOLOGY OF CHROMOSOME

METACENTRIC

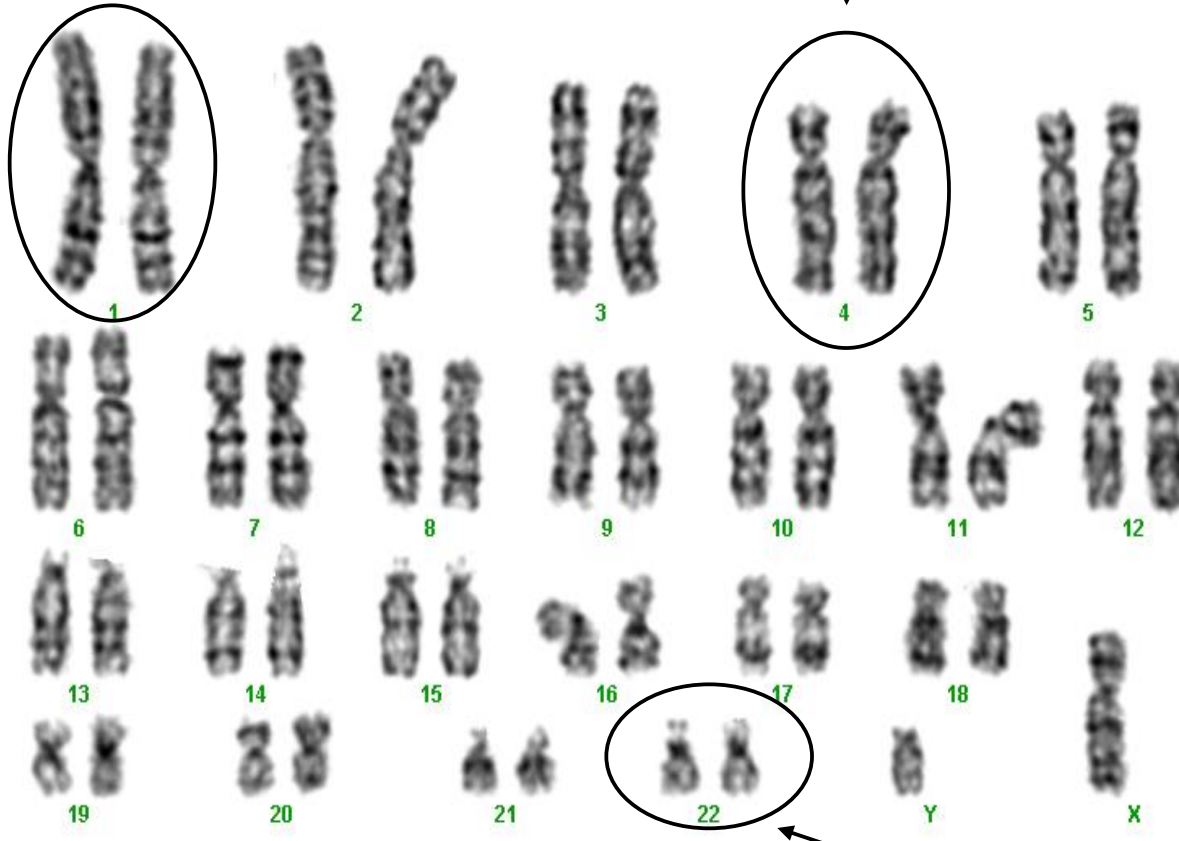
$$p = q$$

SUBMETACENTRIC

$$p < q$$

ACROCENTRIC

$$p \lll q$$



○ KARYOTYPE

- complete set of chromosomes in a species or individual organism,
- describes the number and structure of chromosomes
- in humans: 46,XX (females)
46,XY (males)

- Constitutional karyotype – set of chromosomes one is born with
- Acquired karyotype – e.g. the karyotype of cancer cells

► KARYOGRAM

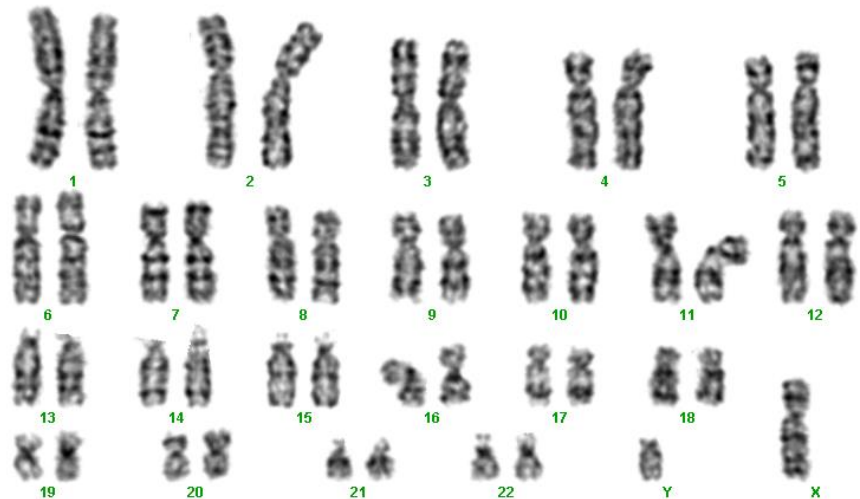
- graphic presentation of karyotype
- chromosomes are ordered by size and a position of centromere

46,XX – female karyotype

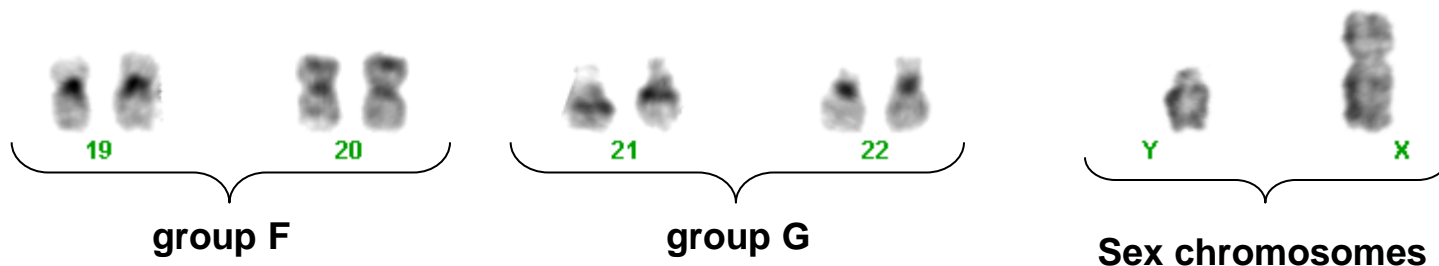
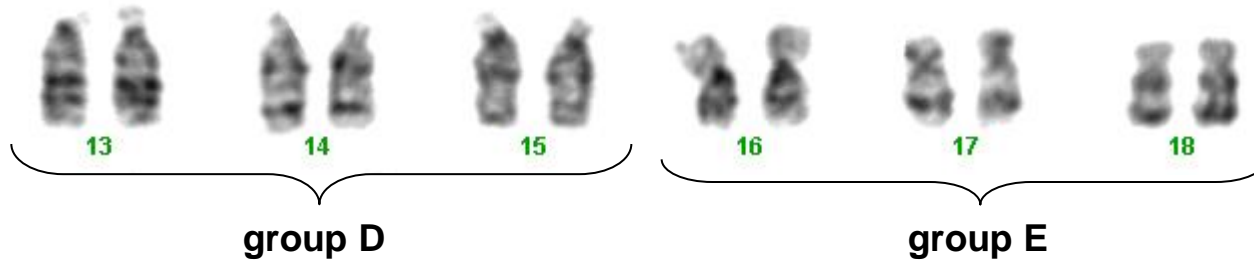
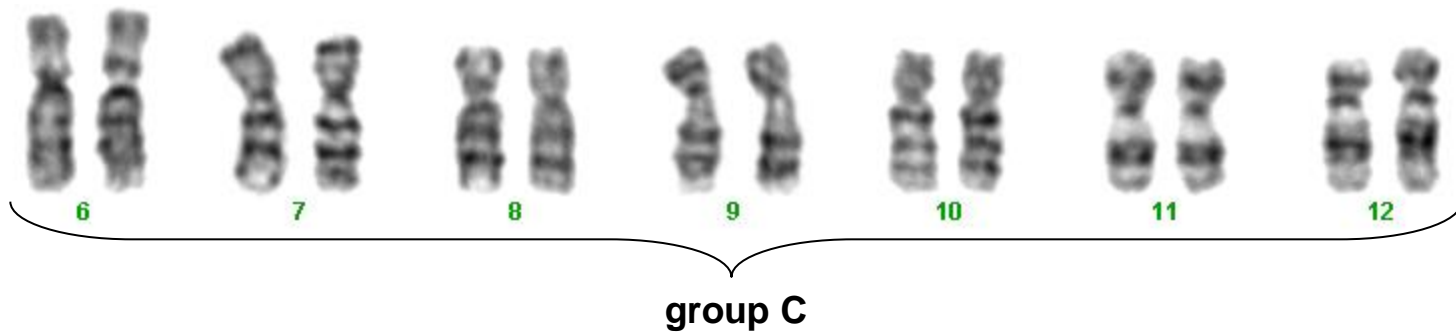
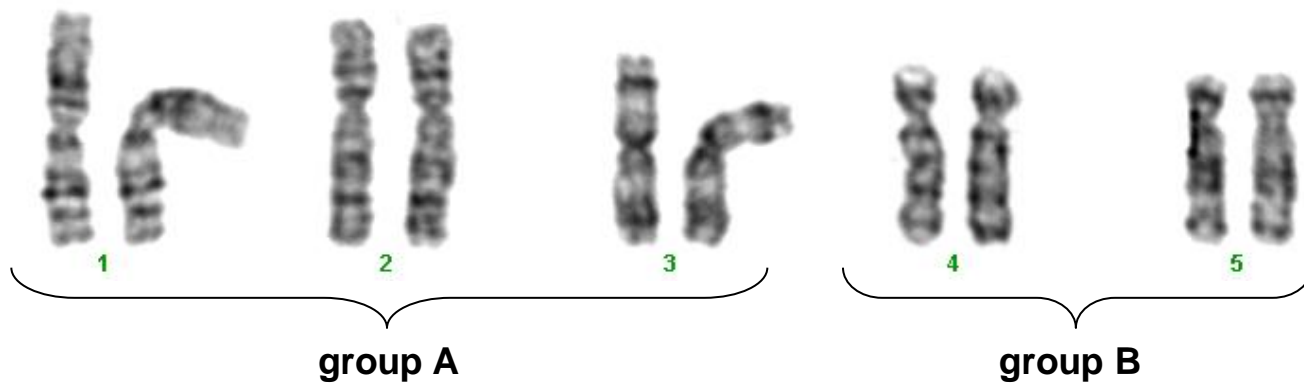


Female karyogram

46,XY – male karyotype



Male karyogram





CHROMOSOMAL ABERRATIONS

37



ABERRATION – every change of number or structure of chromosomes, visible under light microscope.

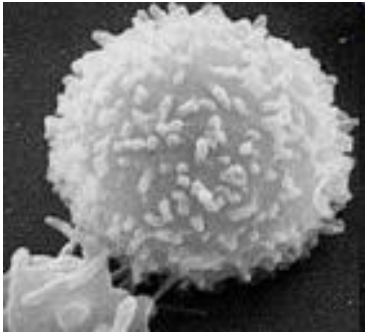
SUBMICROSCOPIC ABERRATION – change undetectable under light microscope, identification possible with techniques of molecular cytogenetics (eg. FISH).



Aberrations occur both in autosomes and sex chromosomes.

Aberrations can originate in somatic cells or in gametes, they can be *de novo* or inherited from one of the parents.

- somatic cells – $2n$ (diploid set) – 46 chromosomes



lymphocyte

- gametes – $1n$ (haploid set) – 23 chromosomes

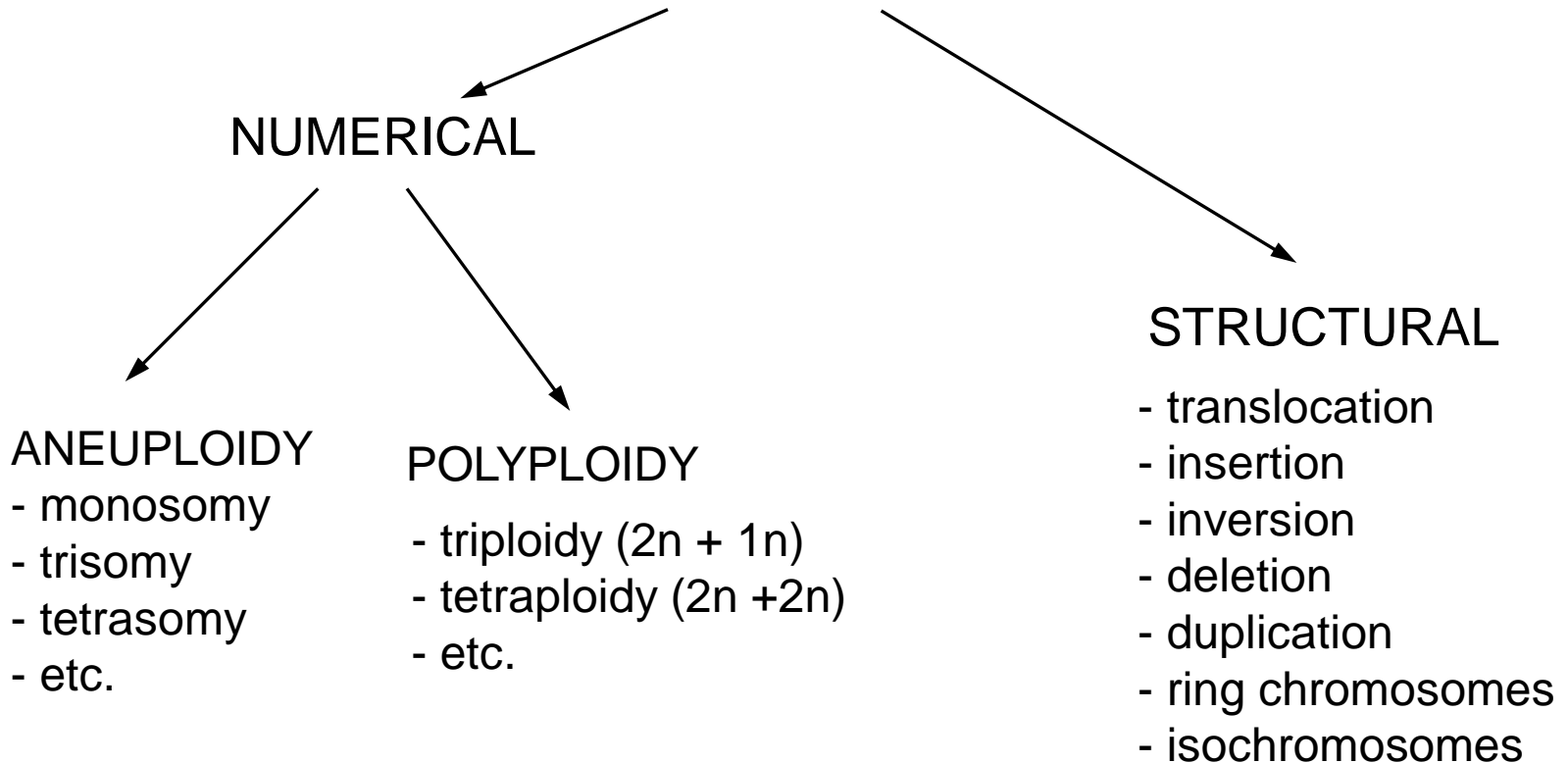


oocyte



sperm cells

CHROMOSOMAL ABERRATIONS



CHROMOSOMAL ABERRATIONS





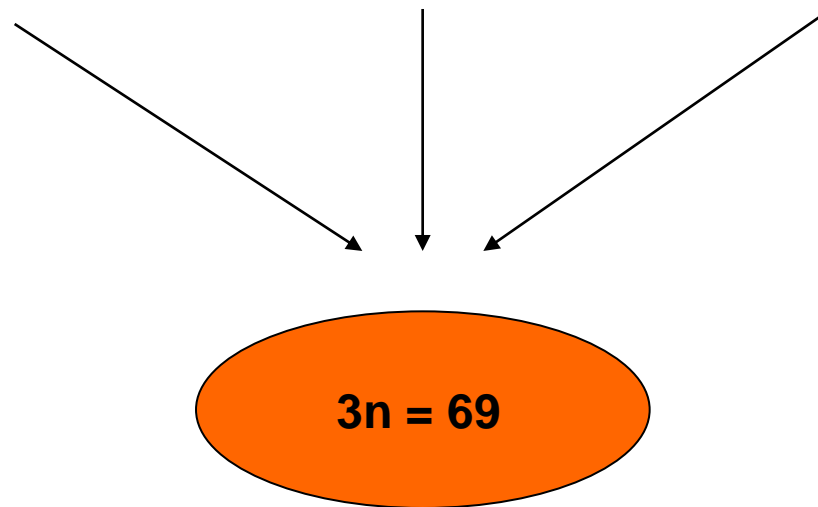
NUMERICAL ABERRATIONS

Normal somatic cells carry 46 chromosomes, normal karyotypes are 46,XX for female and 46,XY for male.

If the number of chromosomes present in cell is exact multiple of haploid number (23) → polyploidy (triploidy, tetraploidy, ...)
eg. 92,XXYY – tetraploidy

Mechanism of formation –

- due to fertilisation of a egg by two sperm cells (dispermy)
- due to absence of division of mature egg cell or sperm cell (it results in formation of diploid gamete).





69,XXY

If the number of chromosomes present in cell is not exact number of haploid set → aneuploidy (monosomy, trisomy, ...)

eg. 45,X – Turner syndrome

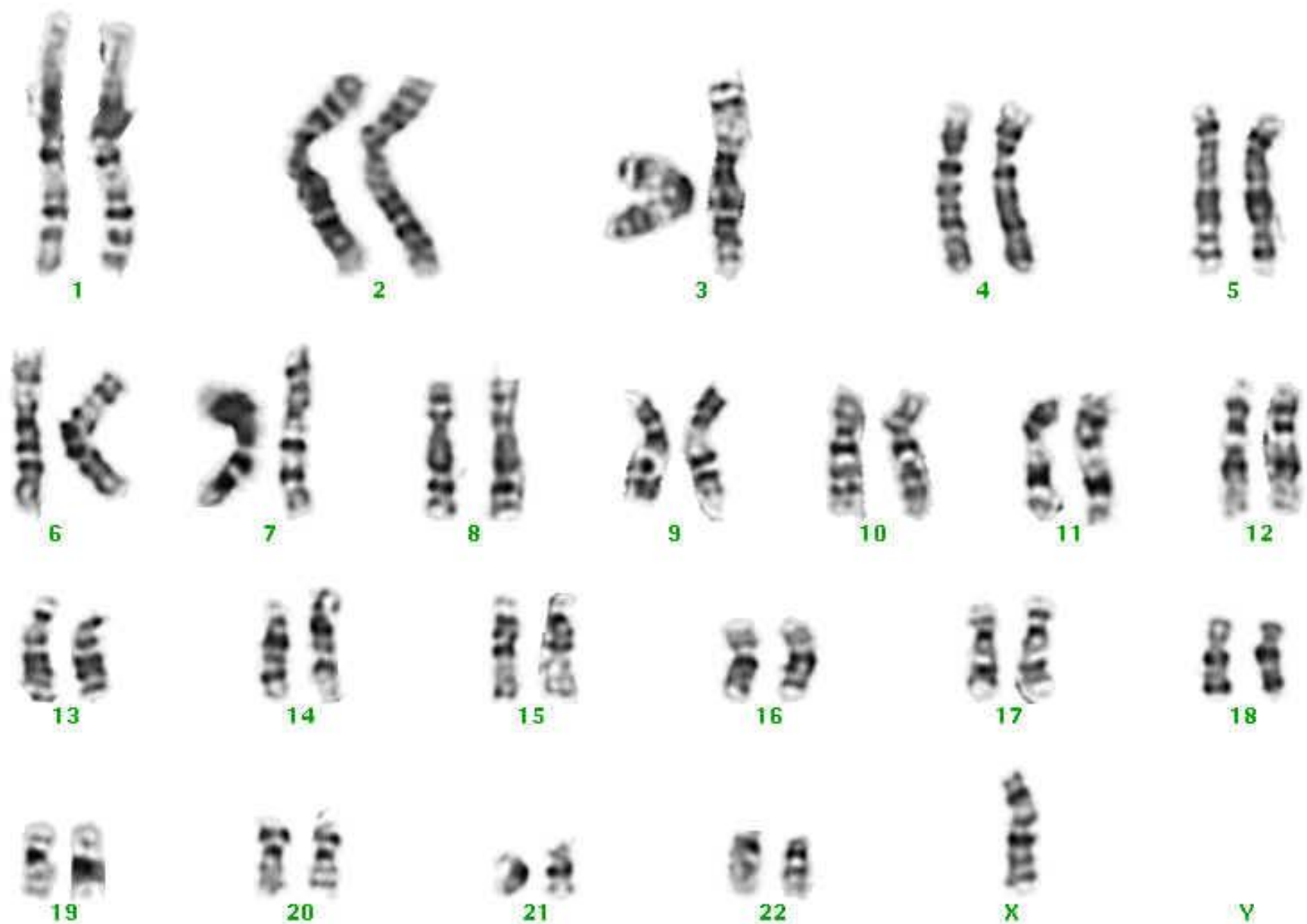
47,XXY – Klinefelter syndrome

47,XX,+18 – Edwards syndrome

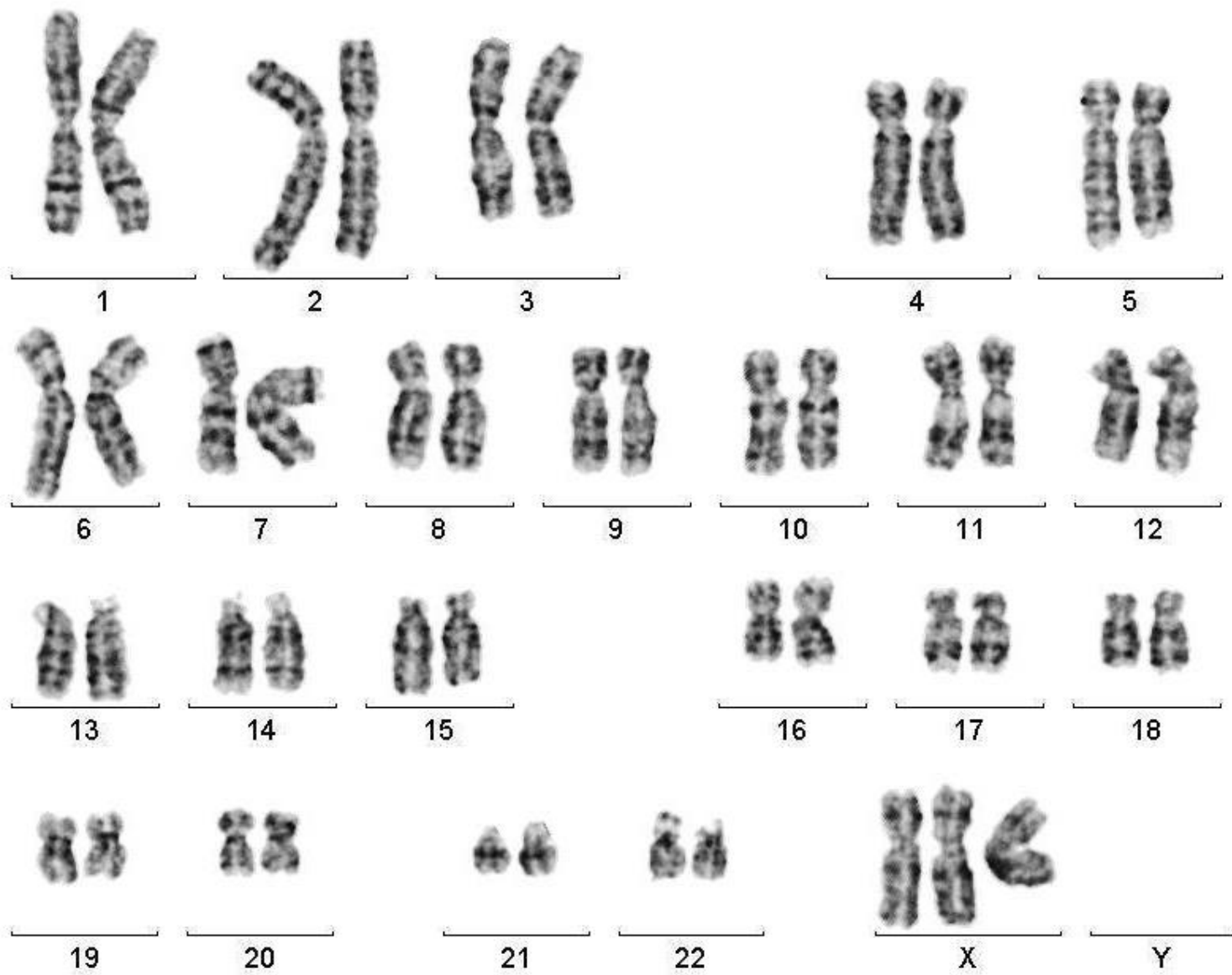
Mechanism of formation – usually as a consequence of faulty separation of pair of chromosomes (or sister chromatids) during anaphase (nondysjunction).

Correlated with maternal age.

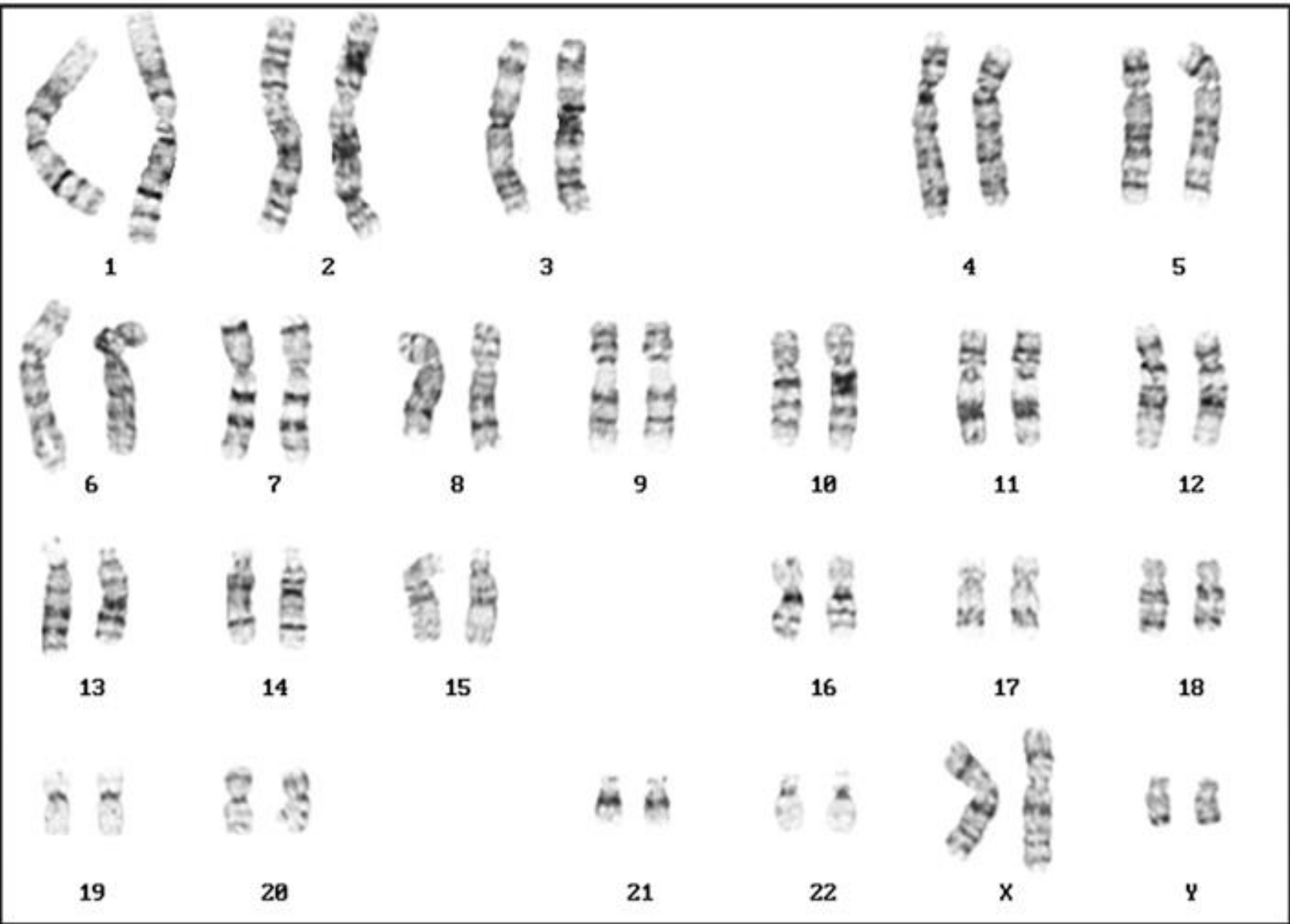
As a result of mitotic aneuploidy MOSAICISM can occur. It is a presence of two (or more) cell populations presenting different chromosomes content.



45,X (Turner syndrome)



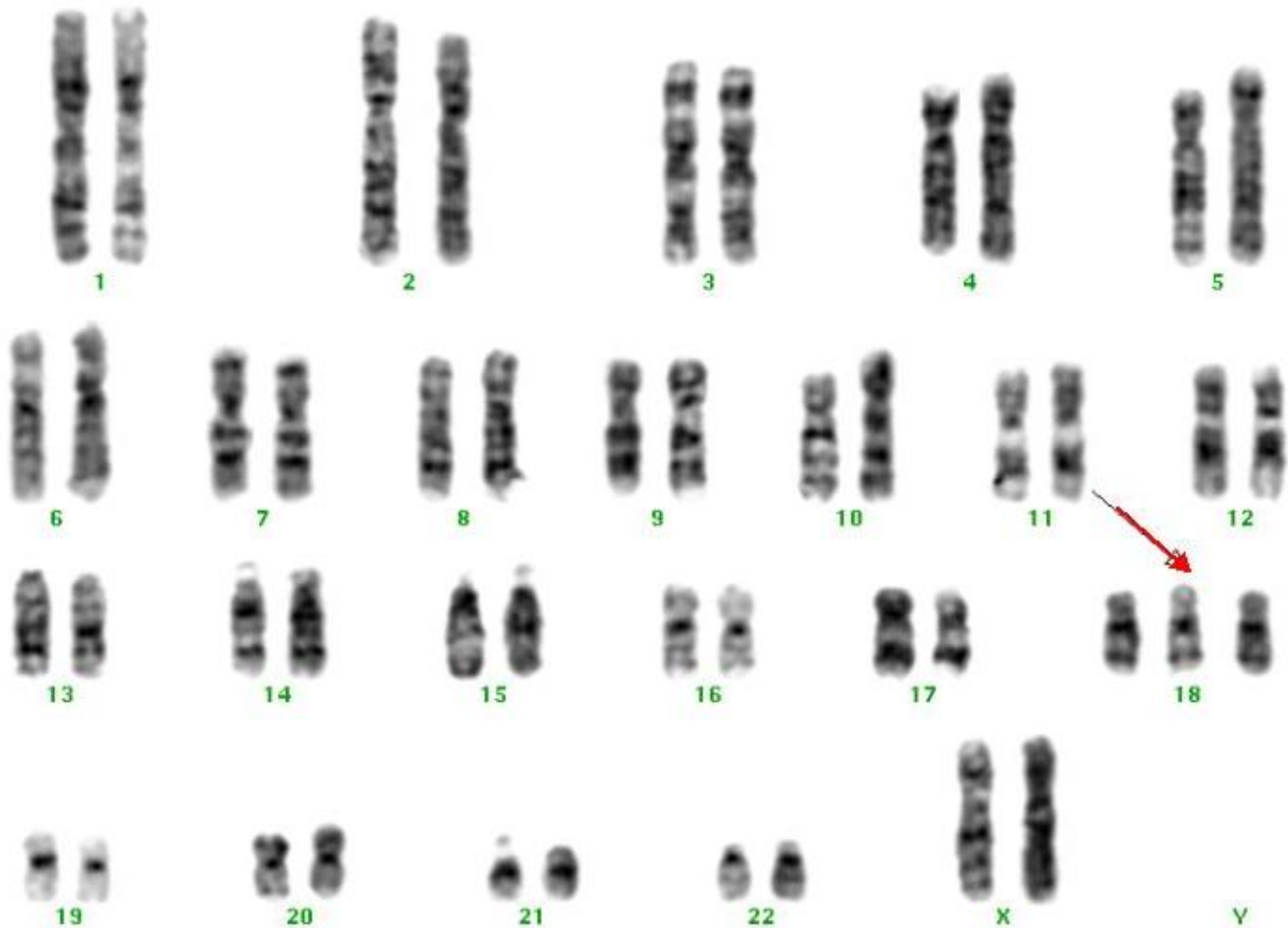
Triple X syndrome – 47,XXX



VARIANT OF KLINEFELTER SYNDROME – 48,XXYY

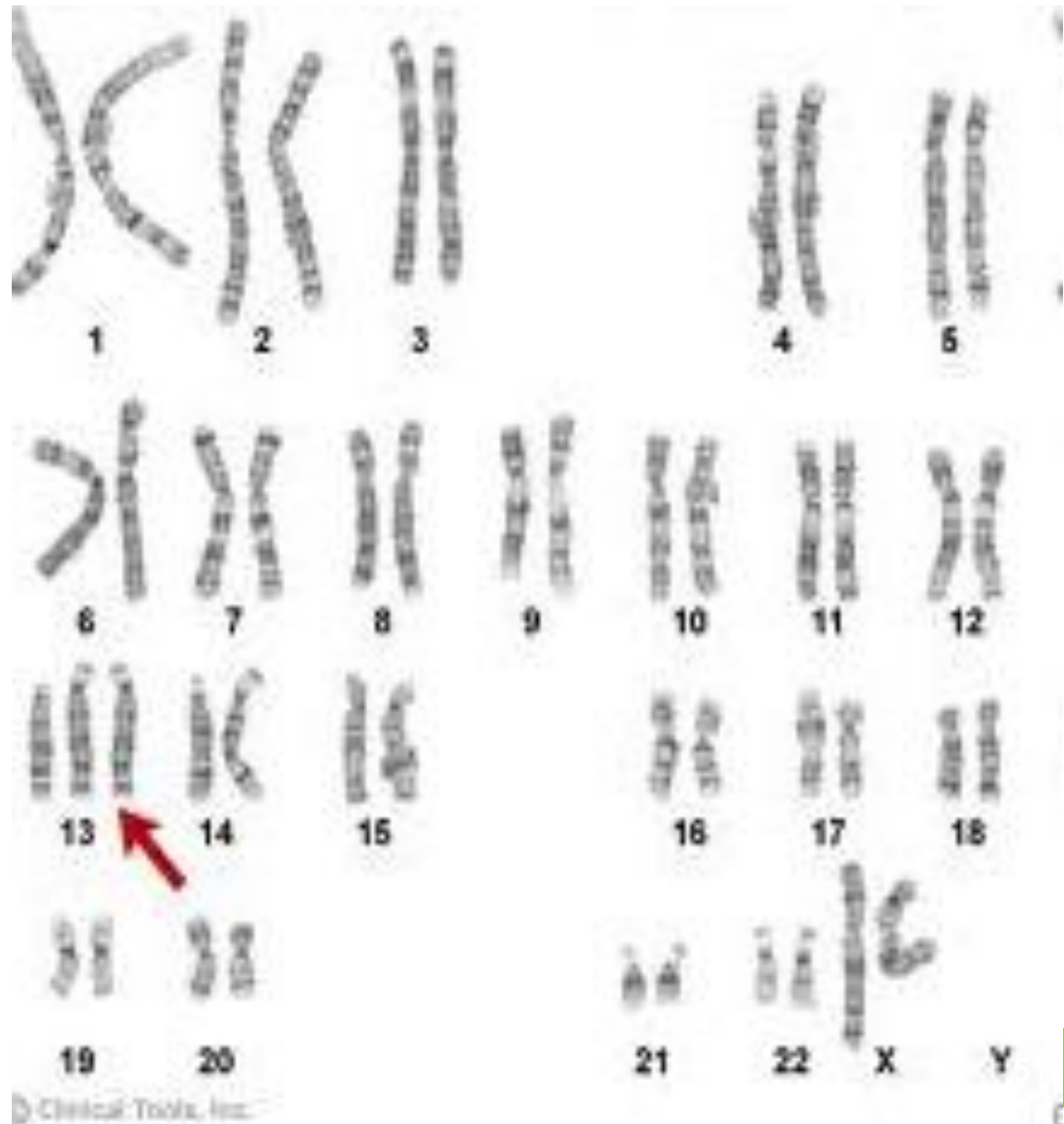


47,XY,+21 (Down syndrome)



Edwards syndrome – 47,XX,+18

PATAU SYNDROME
47,XX,+13



EXAMPLES OF KARYOTYPES WITH NUMERICAL CHANGES

▶ Triploidy ($3n$)

- ▶ 69,XXX
- ▶ 69,XXY
- ▶ 69,XYY

▶ Aneuploidies:

▶ Monosomy ($2n-1$)

- ▶ 45,X
- ▶ 45,XX,-13

▶ Double monosomy ($2n-1-1$)

- ▶ 44,XY,-13,-14
- ▶ 44,X,-X,-18

▶ Nullisomy ($2n-2$)

- ▶ 44,XX,-15,-15
- ▶ 44,XY,-18,-18

▶ Trisomy ($2n+1$)

- ▶ 47,XX,+21
- ▶ 47,XY,+18

▶ Double trisomy ($2n+1+1$)

- ▶ 48,XX,+13,+21

▶ Tetrasomy ($2n+2$)

- ▶ 48,XY,+21,+21



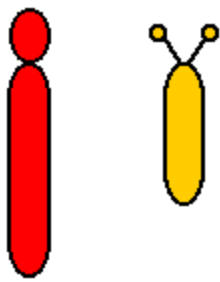
STRUCTURAL ABERRATIONS

All structural changes result from chromosomal breaks.

Where breaks occur, 'sticky ends' are formed. In most of the cases these damages are removed by repair systems.

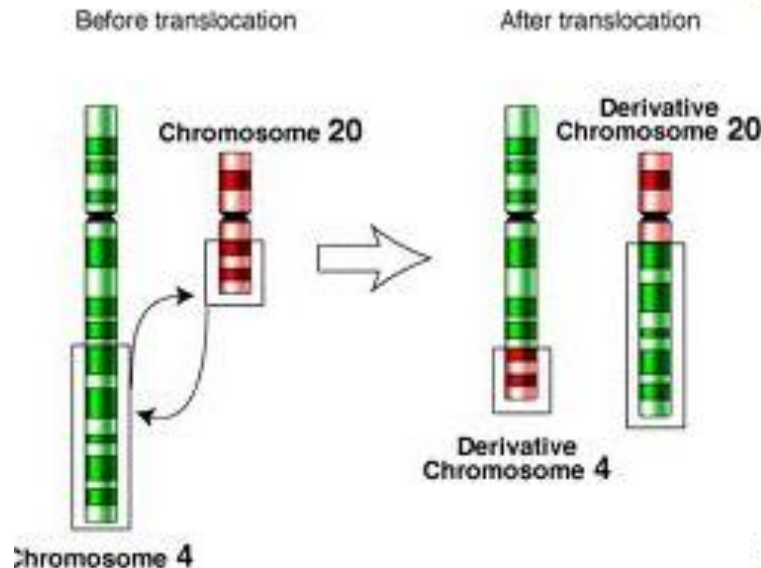
In some cases repair systems do not recognise 'sticky ends' and incorrect joining occurs.

Frequency of spontaneous breaks can rise after an exposure to ionizing radiation, or can be a symptom of some of hereditary diseases.



TRANSLOCATION (t):

- chromosomal abnormality which occurs when chromosomes break and the fragments rejoin to other chromosomes,
- rearrangement of parts between nonhomologous chromosomes,
- reciprocal – usually involves two chromosomes

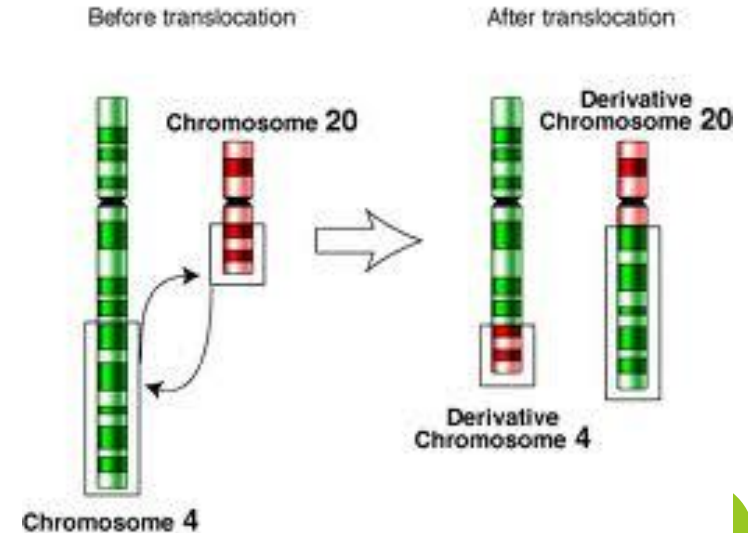
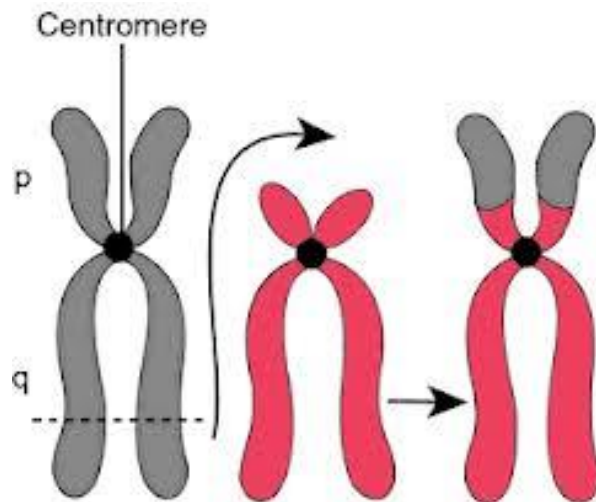
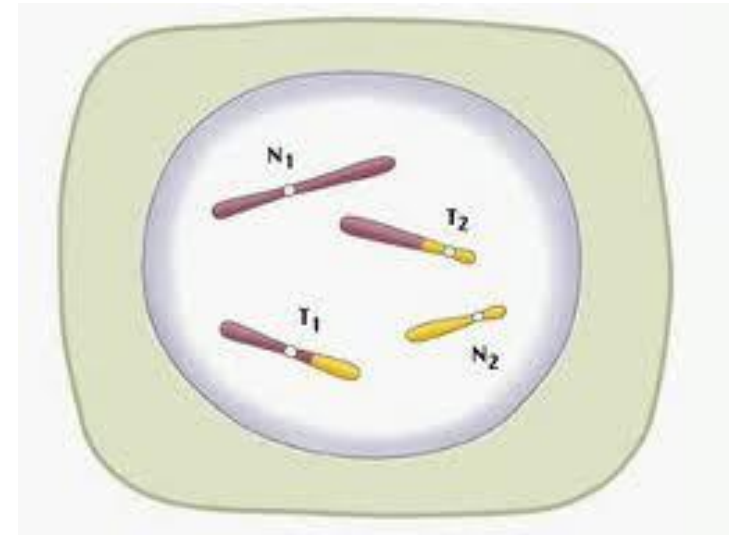




$t(7;11)(p15;q21)$

○ Types of translocations:

- reciprocal
- non-reciprocal
- balanced
- unbalanced



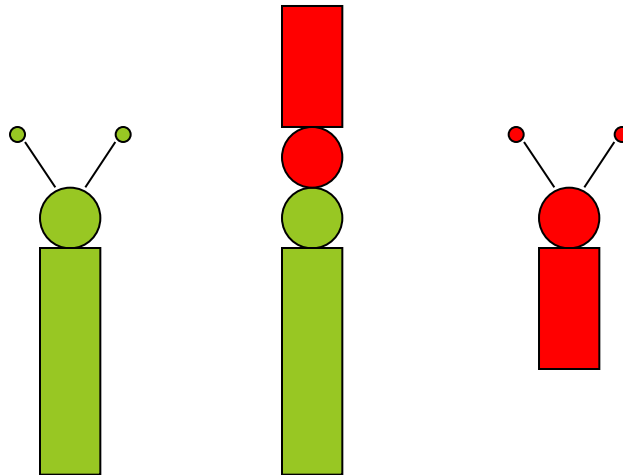
- CENTRIC FUSIONS (ROBERTSONIAN TRANSLOCATIONS)

Occur as a cross-joining of acrocentric chromosomes.

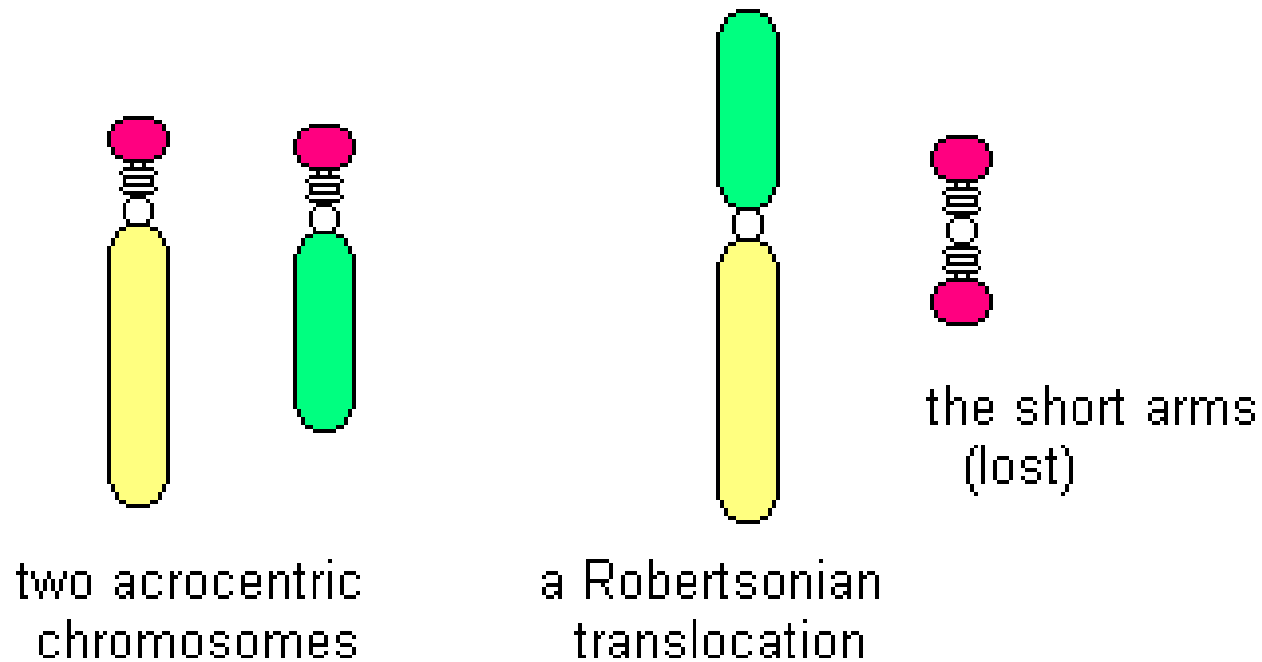
Change usually occurs in centromere, dicentric chromosome can be formed.

Acentric fragment is eliminated from the cell.

Carrier is healthy (no visible clinical symptoms).



CENTRIC FUSIONS (ROBERTSONIAN TRANSLOCATIONS)





1



2



3



4



5



6



7



8



9



10



11



12



13



14



15



16



17



18



19



20



21



22



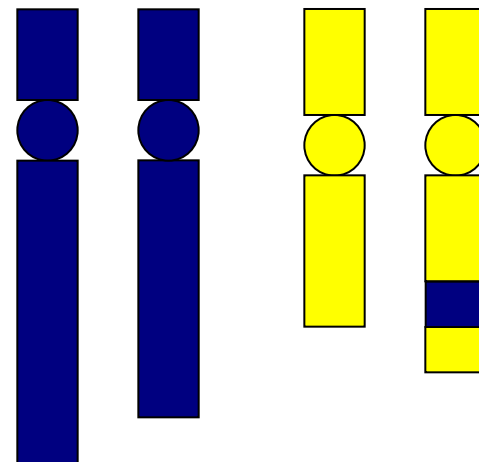
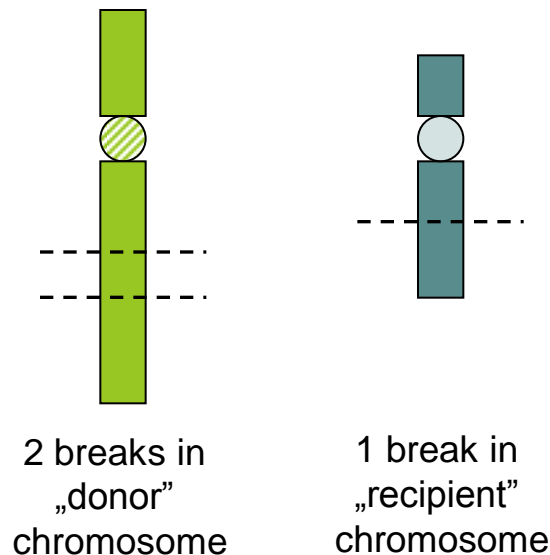
Y



X

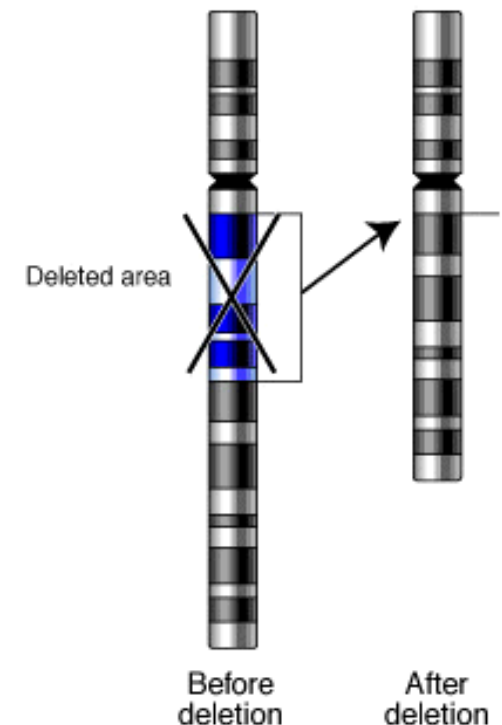
○ INSERTIONS

- special type of translocation,
- non-reciprocal,
- part of one chromosome builds in the structure of another chromosome,
- does not affect carrier,
- can lead to unbalanced karyotype in next generations



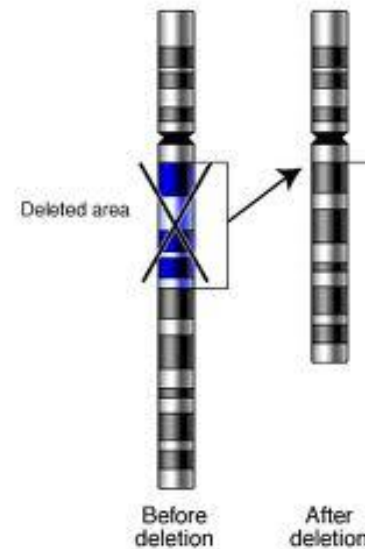
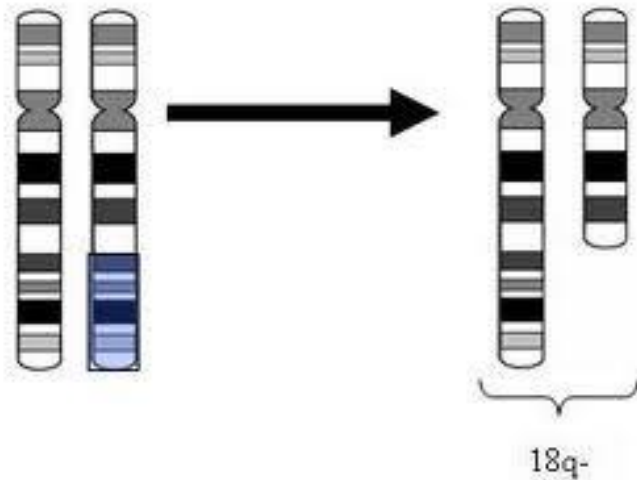
► DELETION (del)

- loss of part of chromosome,
 - any size of deletion can occur,
 - can be caused by errors during crossing-over,
 - can result from a translocation,
 - can be caused by breaking without rejoining
-
- interstitial deletions (within an arm),
 - terminal deletion (at the end of p or q arm)
-
- large in size are usually fatal.



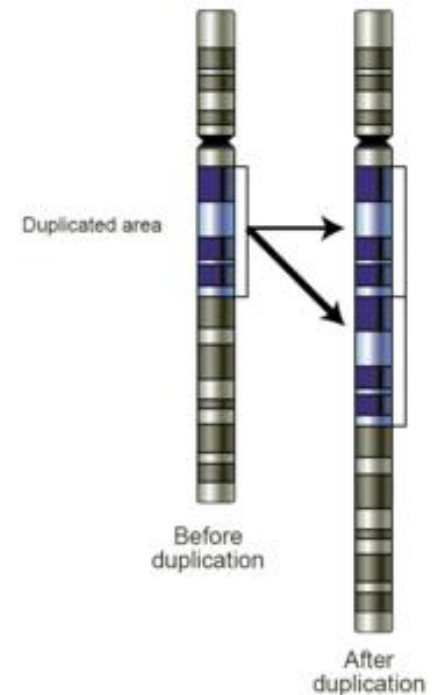
○ Types of deletions:

- Terminal – affects terminal sequences (p or q arm)
- Interstitial – within one arm (p or q)



► DUPLICATION (dup)

- duplication of any region of chromosome
- may occur due to recombination error
- arise from an unequal crossing-over between misaligned homologous chromosomes
- may result from a translocation

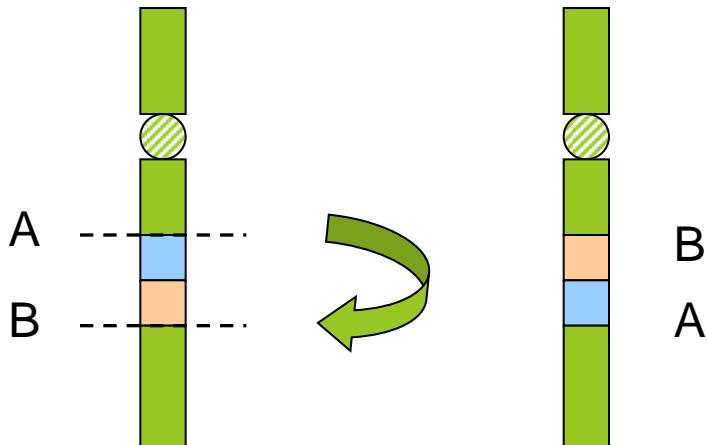


○ INVERSION (inv)

- occurs when a single chromosome undergoes breakage and rearrangement within itself,
- usually do not cause any abnormalities in carriers as long as the rearrangement is balanced with no extra or missing genetic information.

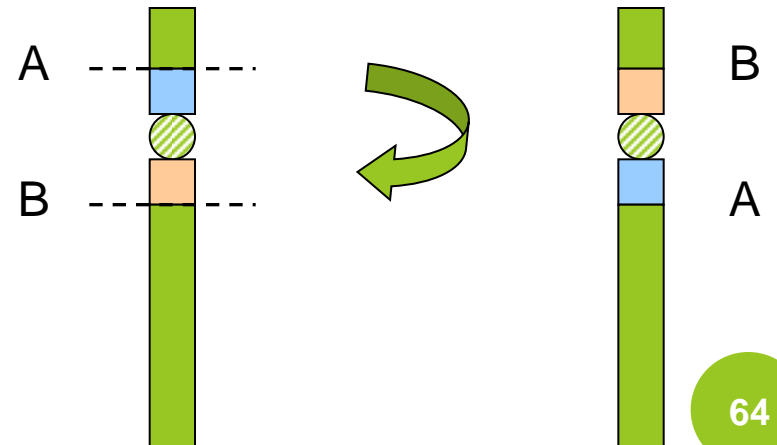
PARACENTRIC INV

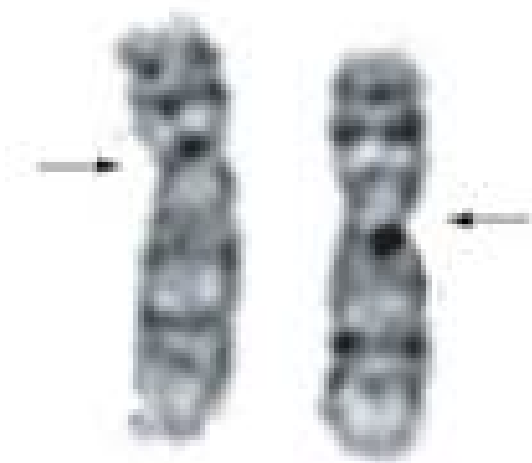
- do not include centromere
- both breaks occur in one arm



PERICENTRIC INV

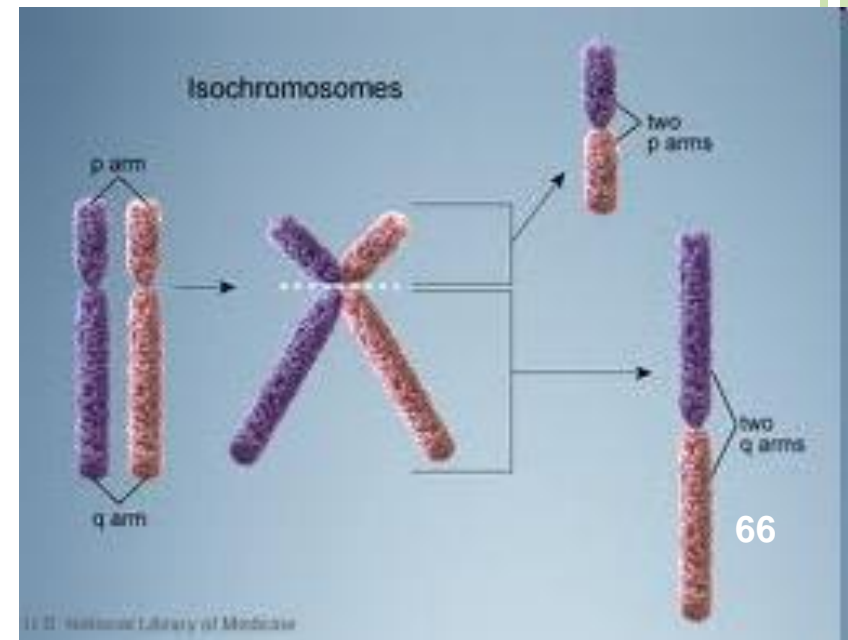
- includes centromere
- breaks in both arms (p and q)



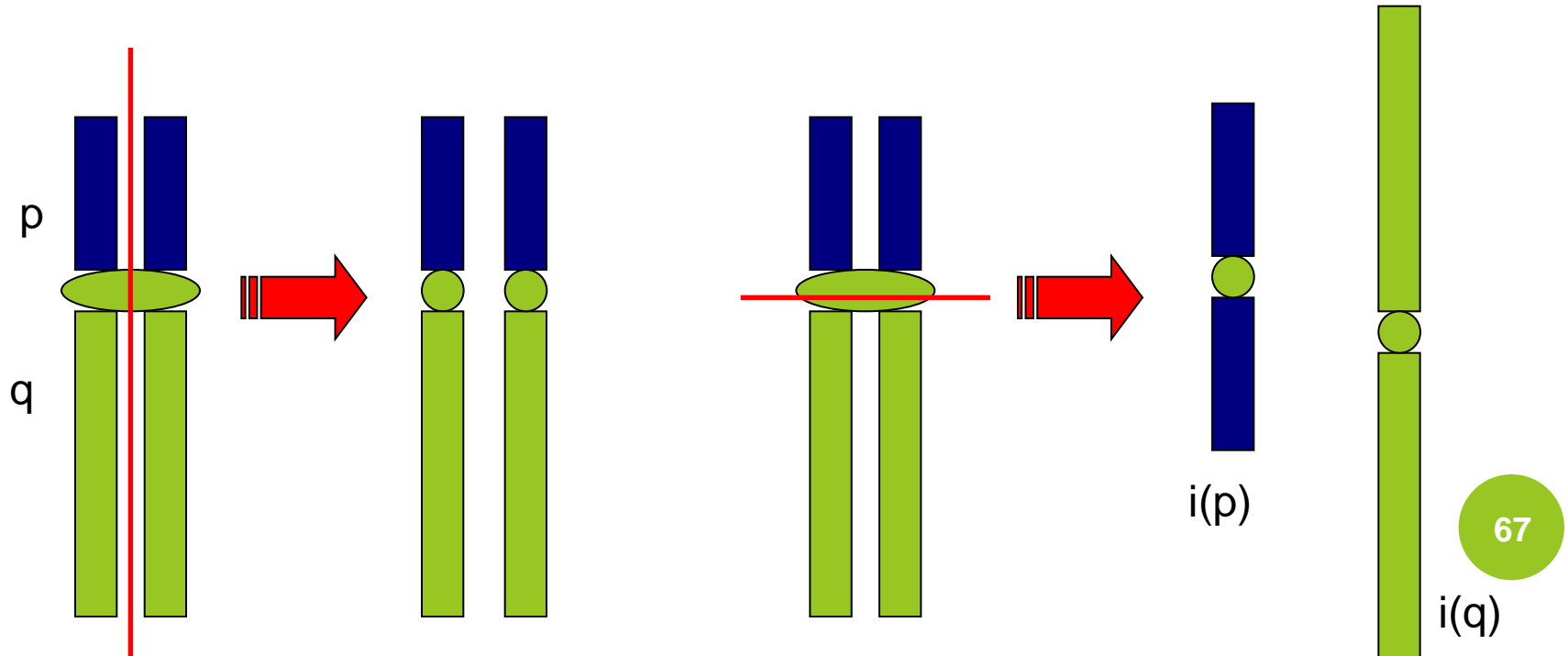


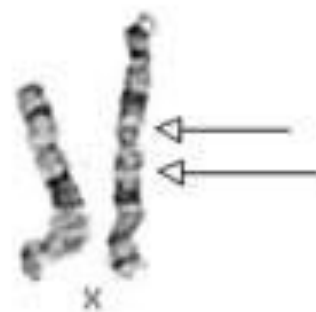
○ ISOCHROMOSOMES (i)

- Special type of both deletion and duplication occurring in one event
- Disruption in a centromere
- Acentric fragments are removed from a cell
- i(21q) is the most frequent isochromosome



- An abnormal chromosome with deletion of one arm and duplication of the other arm.
- Can arise due to transverse division of centromere.
- Frequently $i(Xq)$ and $i(Yq)$.

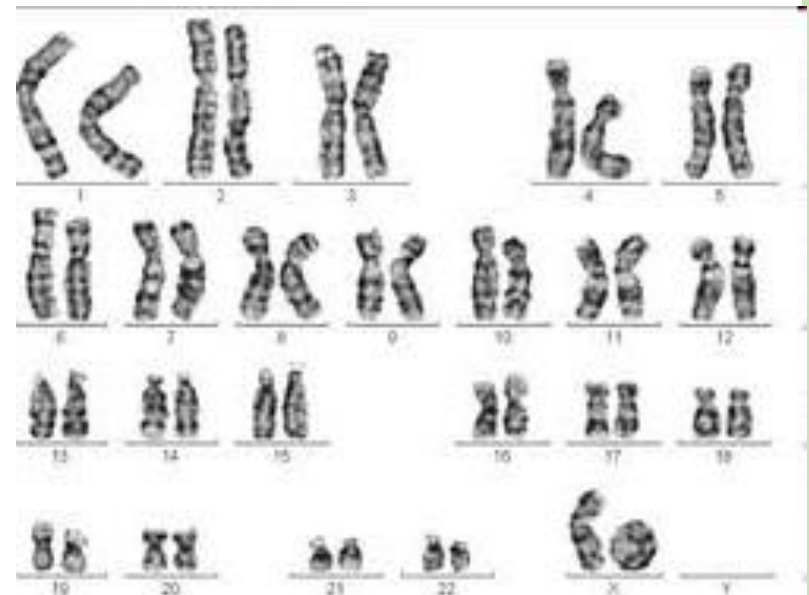
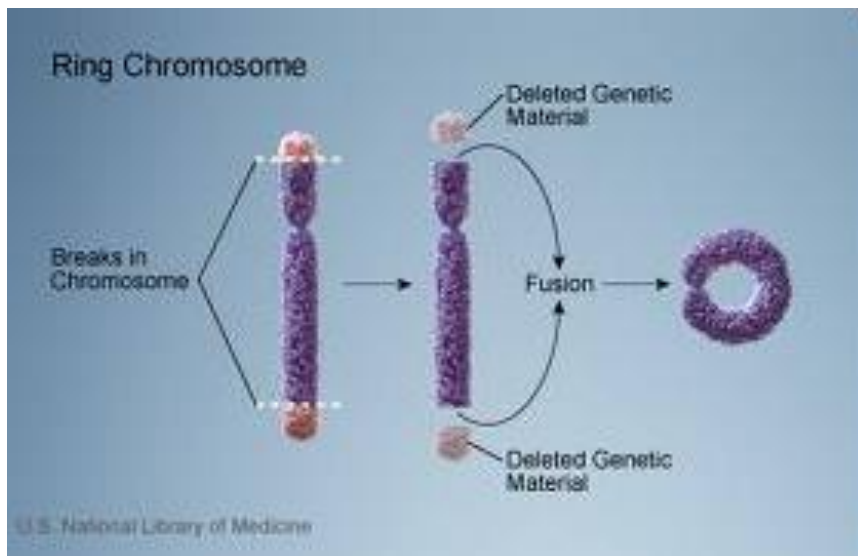




46,X,i(X)(q10)

○ RING CHROMOSOMES (r)

- special type of distal deletion of both arms
- „sticky ends” bind together



○ Congenital aberrations = constitutional

- chromosomal abnormalities occurring in all cells or only in some cell lines of the body
- aberrations present from the moment of conception or arising at a very early stage of embryogenesis

○ Acquired aberrations:

- chromosome abnormalities acquired during the patient's life
- most often concern as changes in cancer tissues