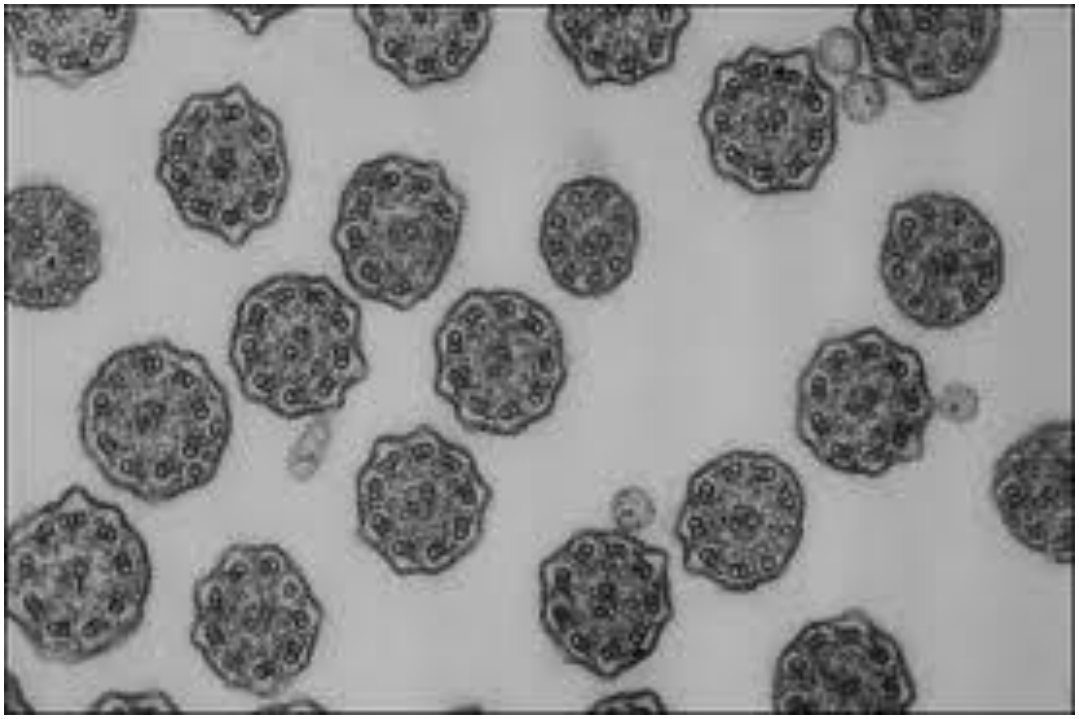
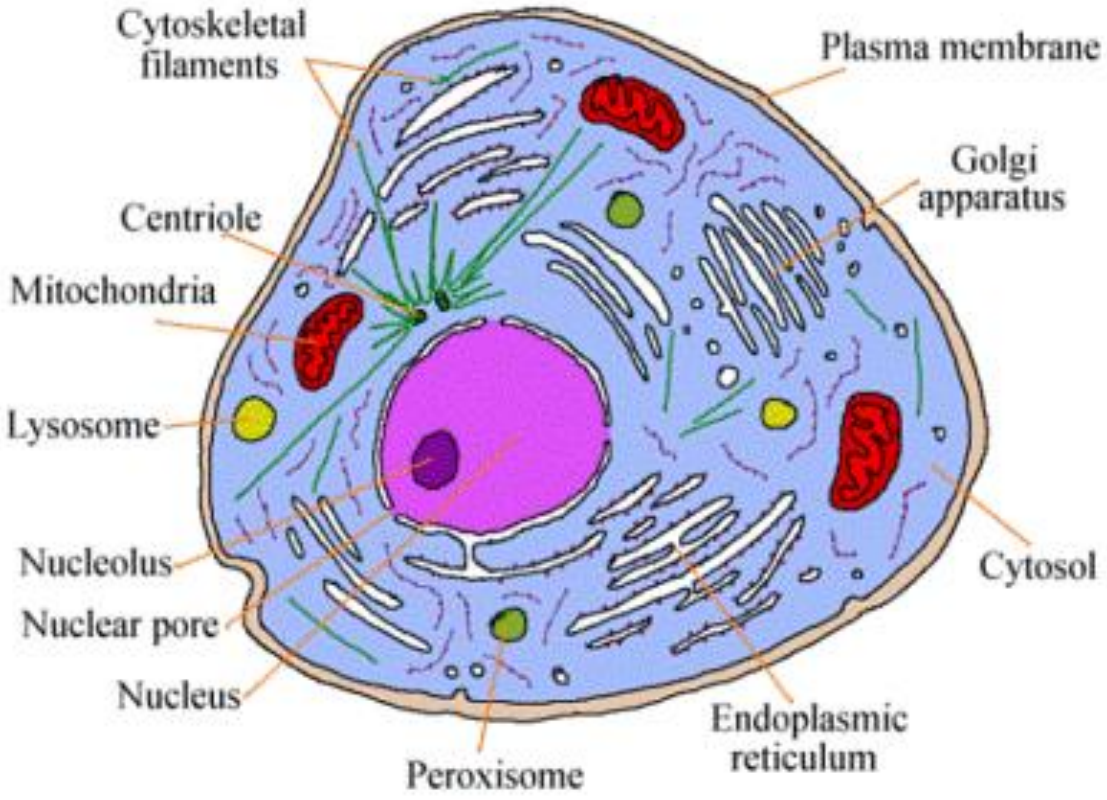


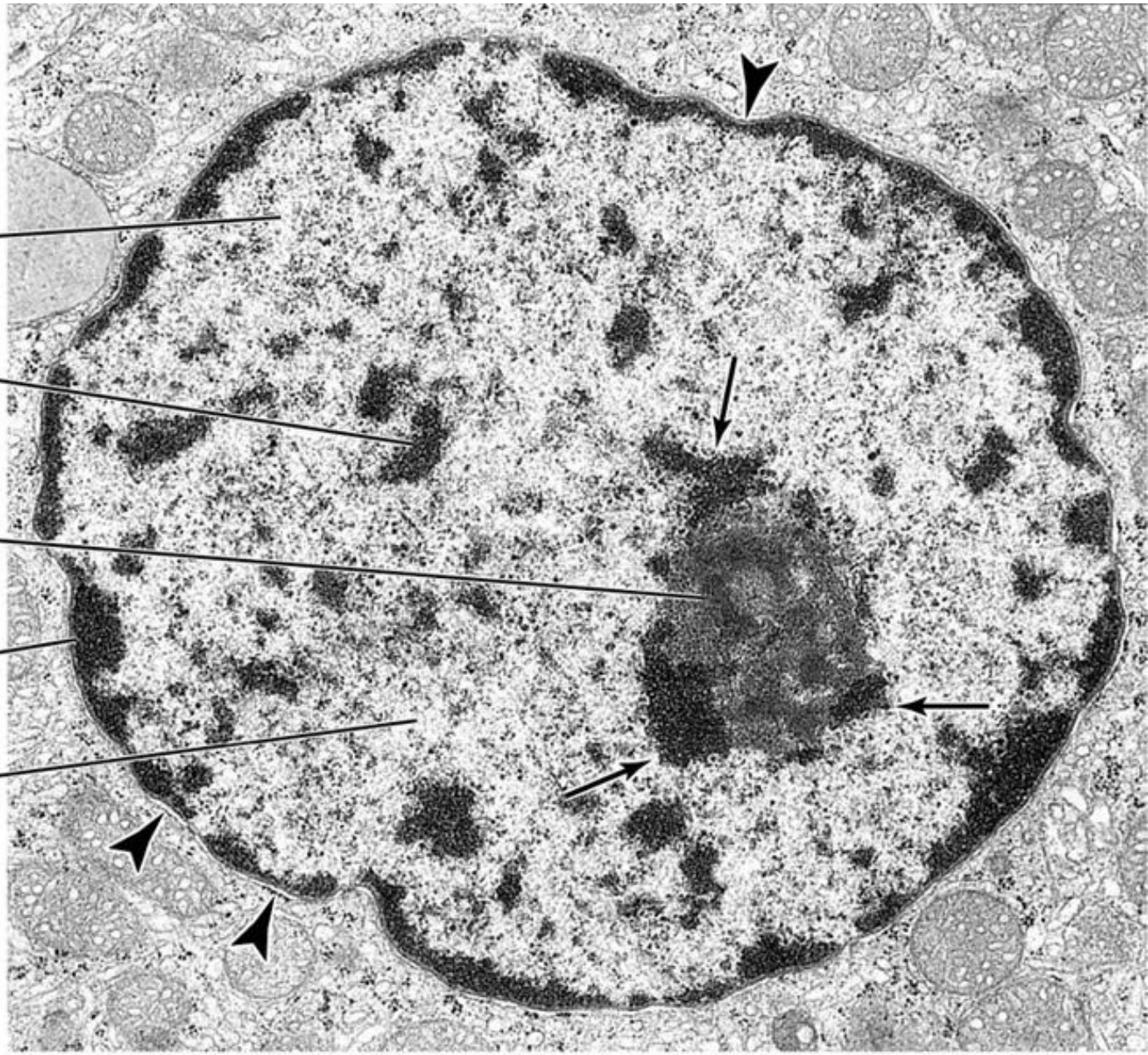
NUCLEUS ULTRASTRUCTURE
CELL DIVISION

NUCLEUS - the largest organelle of the cell

The main function of the cell nucleus is to control of gene expression and mediate the replication of DNA during the cell cycle.



Cell nucleus in electron microscope

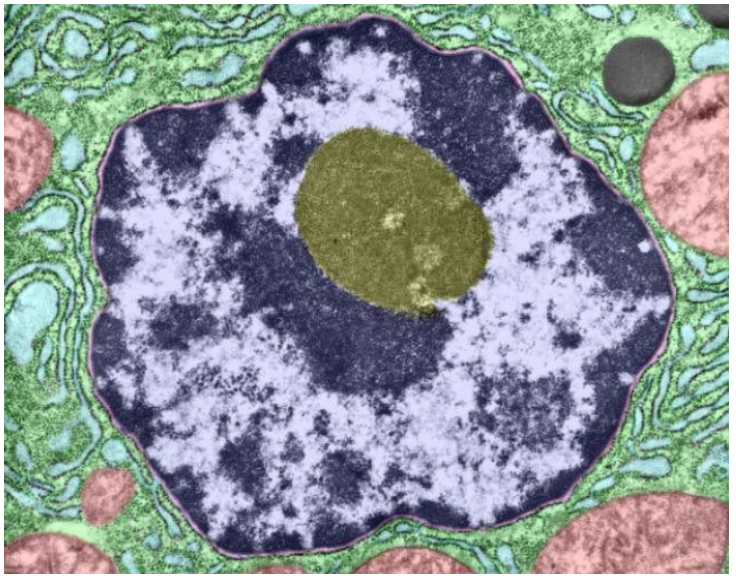


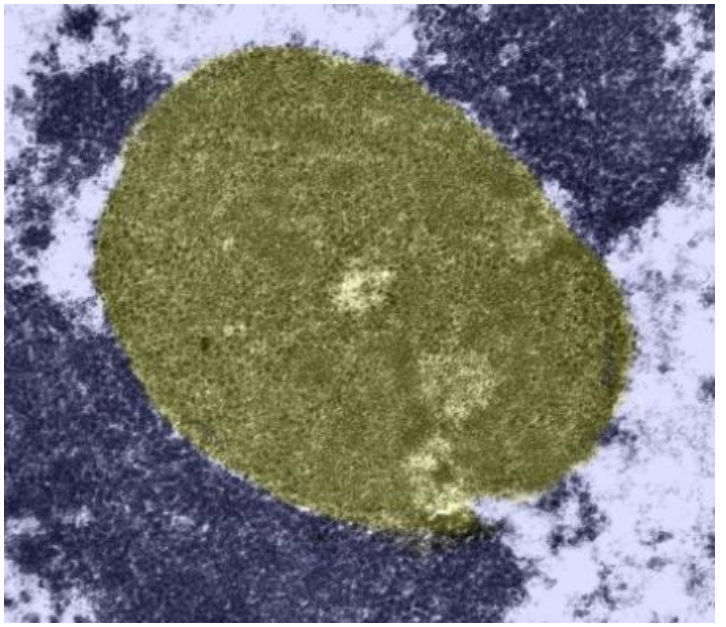
Nucleolus

- There may be 1 to 5 nucleoli in the nucleus

- Nucleolus contains genes necessary for ribosome production

- these genes come from chromosome 13, 14, 15, 21 and 22 (NOR)



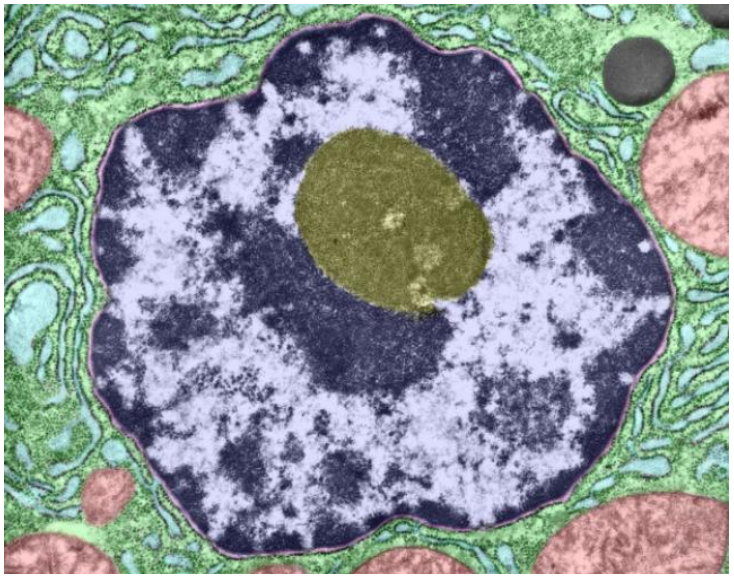


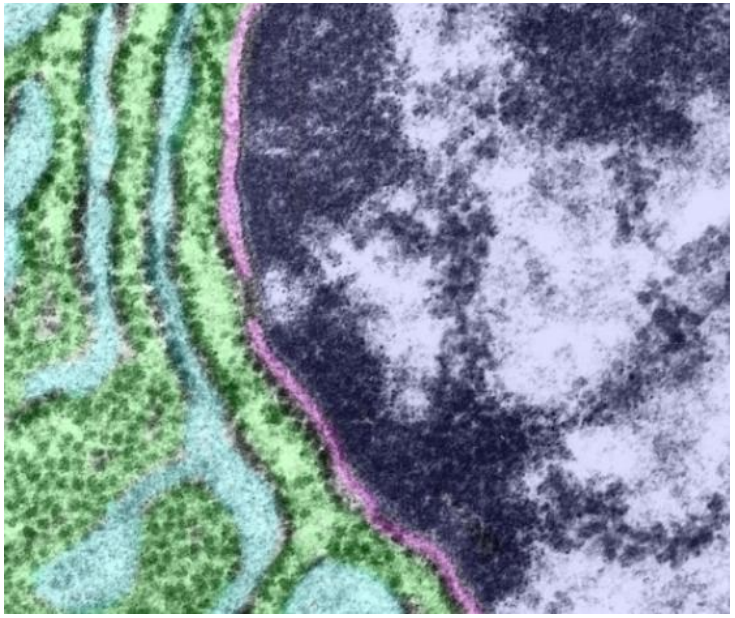
Nuclear envelope

Outer nuclear membrane

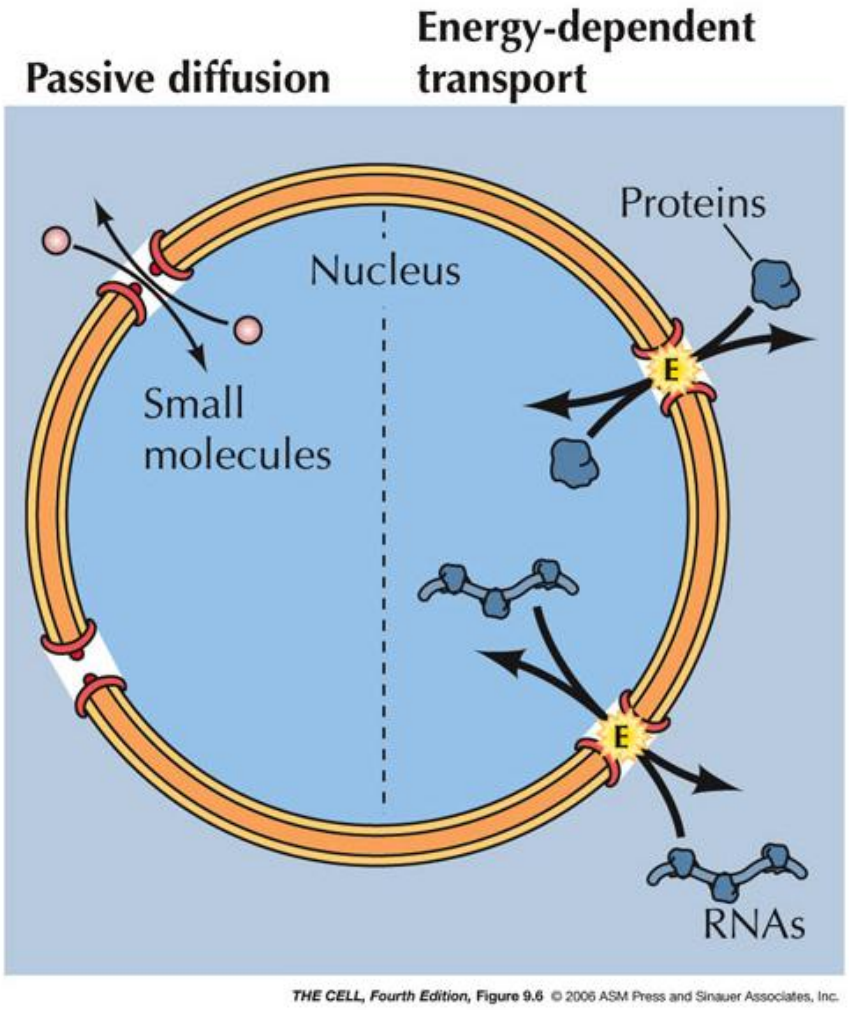
Inner nuclear membrane:

Separated from nuclear material by the **nuclear lamina**





Nuclear pore

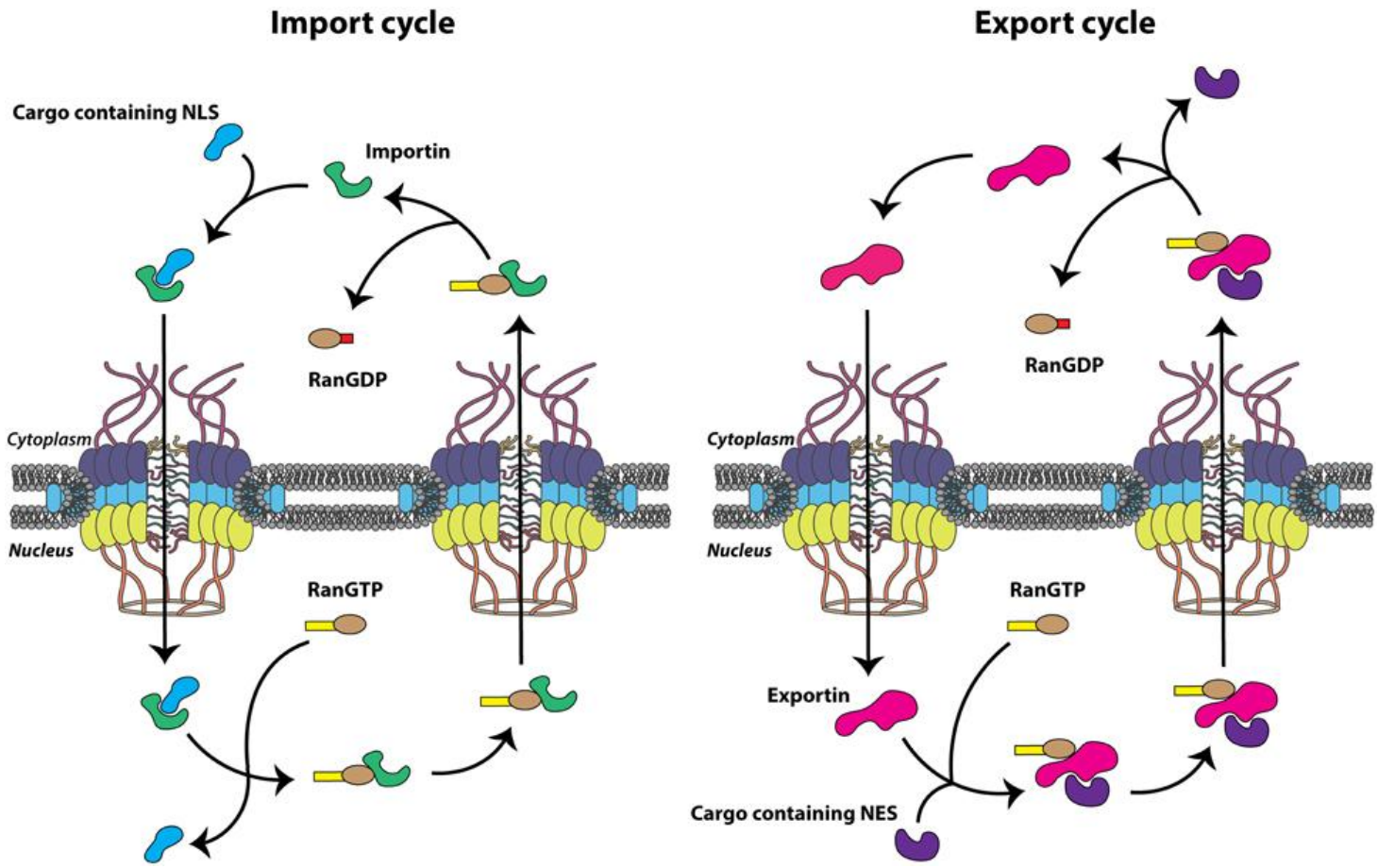


THE CELL, Fourth Edition, Figure 9.6 © 2006 ASM Press and Sinauer Associates, Inc.

http://histologyguide.org/

Recycling of nuclear transport receptors (importin (green) and export (pink)), through a nuclear pore complex - (GTP hydrolysis).

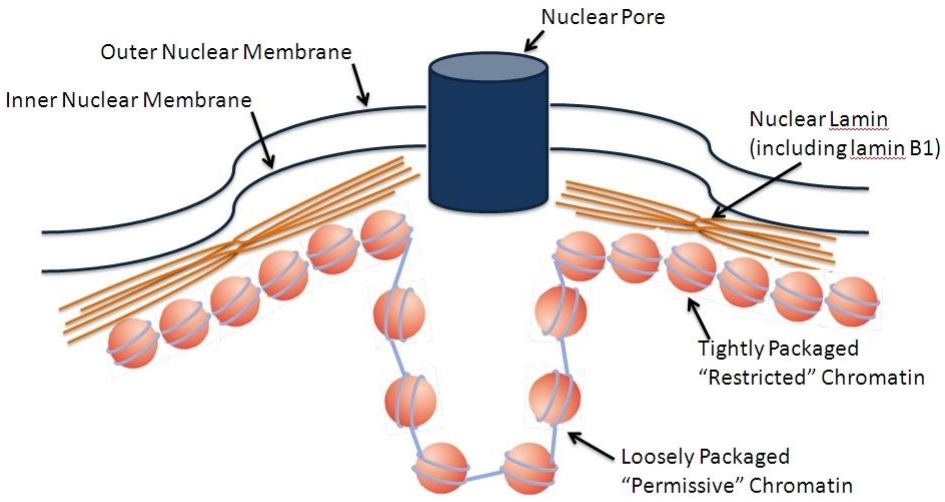
Imported particles: Nuclear Location Signal (NLS) (light blue) or Nuclear Export Signal (NES) (purple).



Flather D. et al.; Picornaviruses and nuclear functions: targeting a cellular compartment distinct from the replication site of a positive-strand RNA virus; Front. Microbiol., 2015

Nuclear lamina - lamins

During interphase, chromatin in the nucleus is divided into **chromosome territories** and anchored to the nuclear lamina



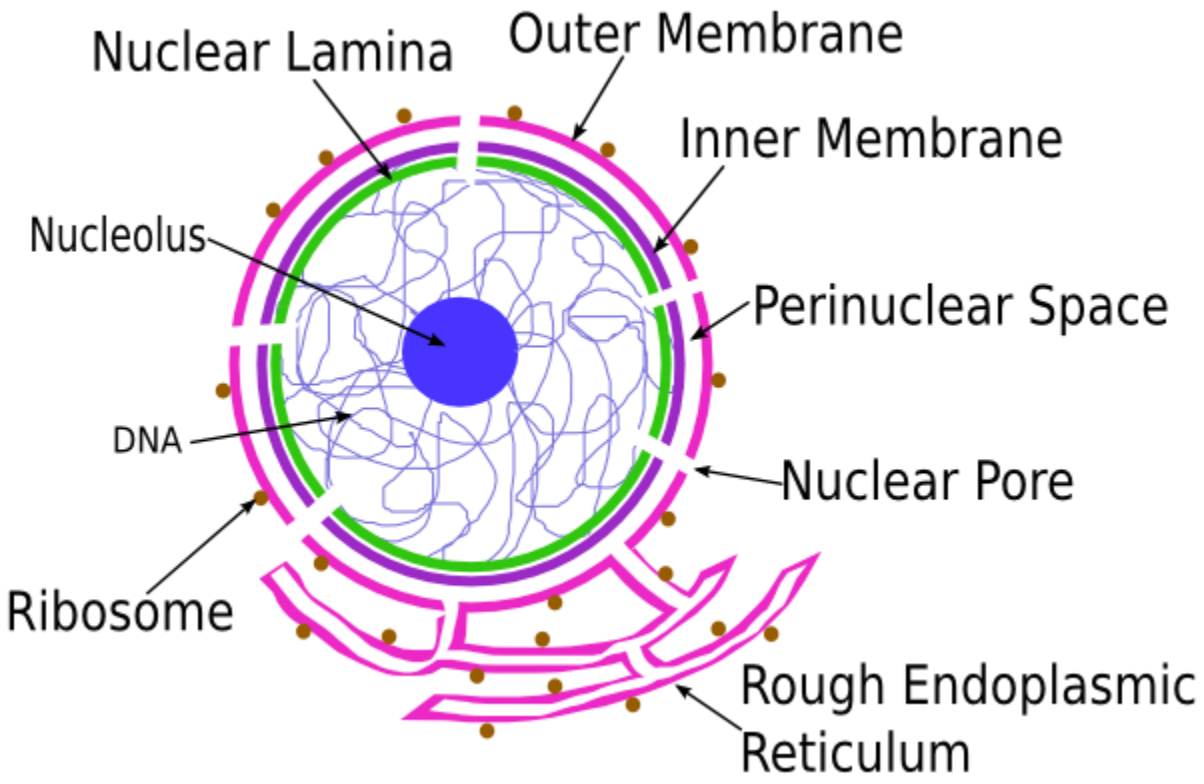
Adapted from Kind and van Steensel, *Curr Opin Cell Biol*

Lamins are regulators of chromatin position. Transcriptionally silent regions of the genome, such as centromeres, telomeres, and the inactive X chromosome, are preferentially located beneath the nuclear lamina

Owen K. et al., Chromatin Structure and Replication Origins: Determinants of Chromosome Replication and Nuclear Organization, In Journal of Molecular Biology, 2014

Bas van Steensel et al.; Genomics tools for unraveling chromosome architecture; Nature Biotechnology;2010

Laminopathies are a group of genetic disorders caused by mutations in genes encoding proteins of the nuclear lamina.

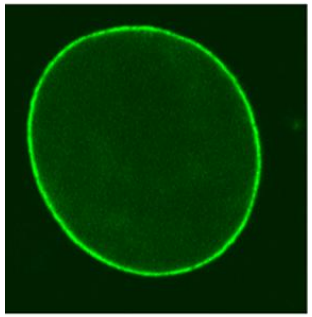


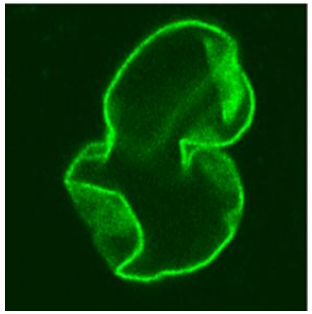
Emery-Dreifuss muscular dystrophy - A muscle wasting disease

Progeria - Premature aging

Restrictive dermopathy - A disease associated with extremely tight skin and other severe neonatal abnormalities

Hutchinson Gilford Progeria Syndrome





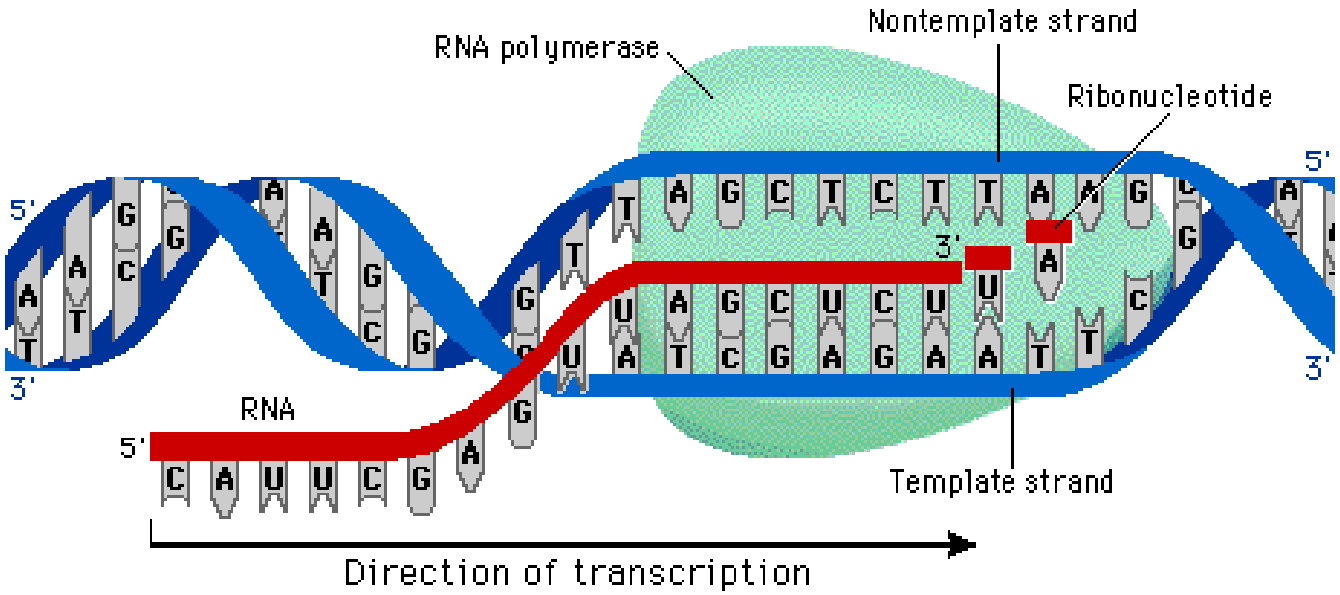
normal fibroblast and of fibroblast of patient with progeria.

Extremely rare genetic disease, symptoms resembling aging are manifested during their first few months after birth. The average life expectancy for a child with progeria is about 13 years.

Symptomes: Scleroderma-like skin condition, limited growth and full-body alopecia (hair loss), atherosclerosis, kidney damage, loss of eyesight, and cardiovascular problems. People diagnosed with this disorder usually have small, fragile bodies, like those of elderly people.

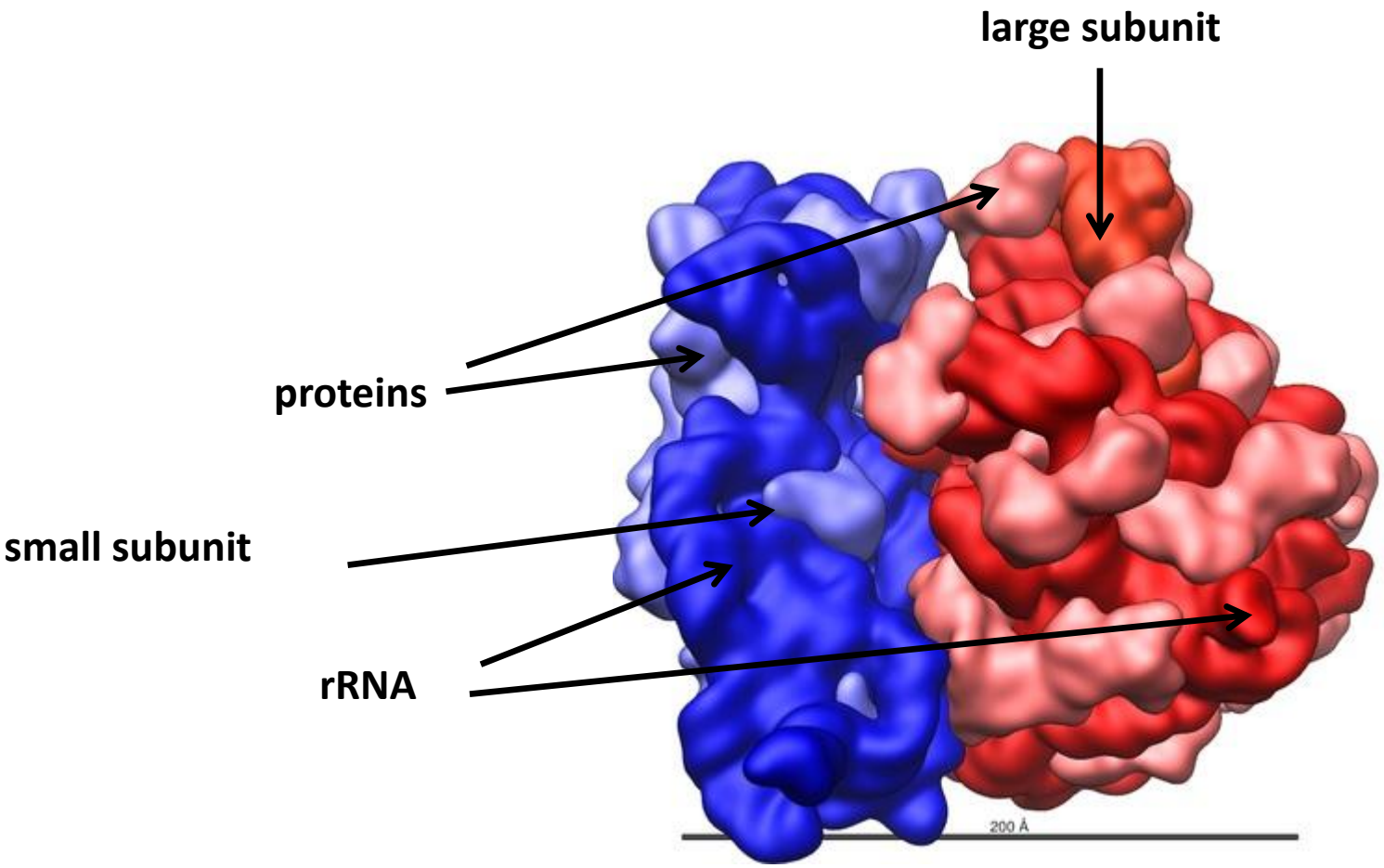
TRANSCRIPTION

- DNA sequence is read by an RNA polymerase, which produces a complementary, antiparallel RNA strand. New-formed RNA contains uracil (U) instead of thymine (T) presented in DNA.



Ribosomal RNA (rRNA)

- rRNA is produced **nucleolus** by RNA polymerase I.



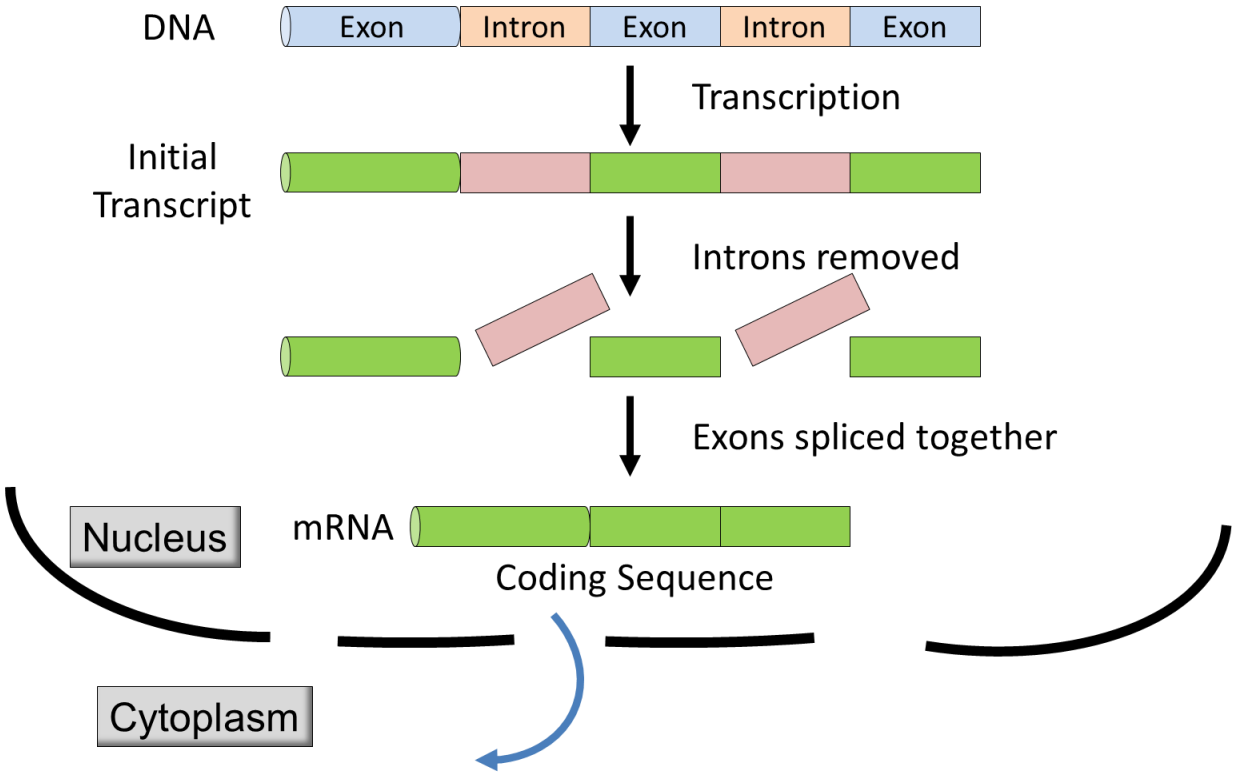
Messenger RNA (mRNA)

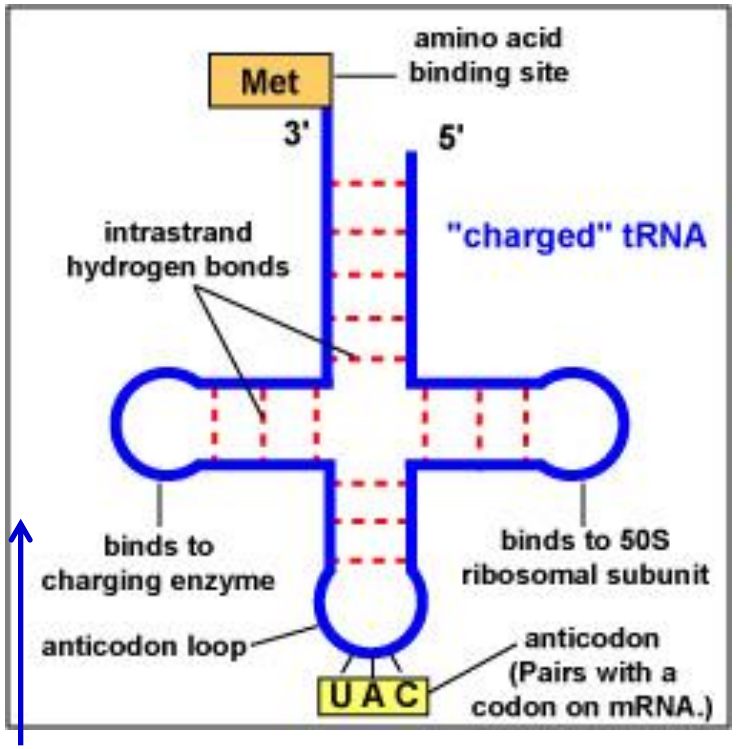
Produced from DNA by RNA polymerase II

- It is complementary copy of one gene

- contains coding segments - exons and noncoding segments – introns. Introns must be removed, exons must be spliced together.

- After processing mRNA is transported into cytoplasm. .





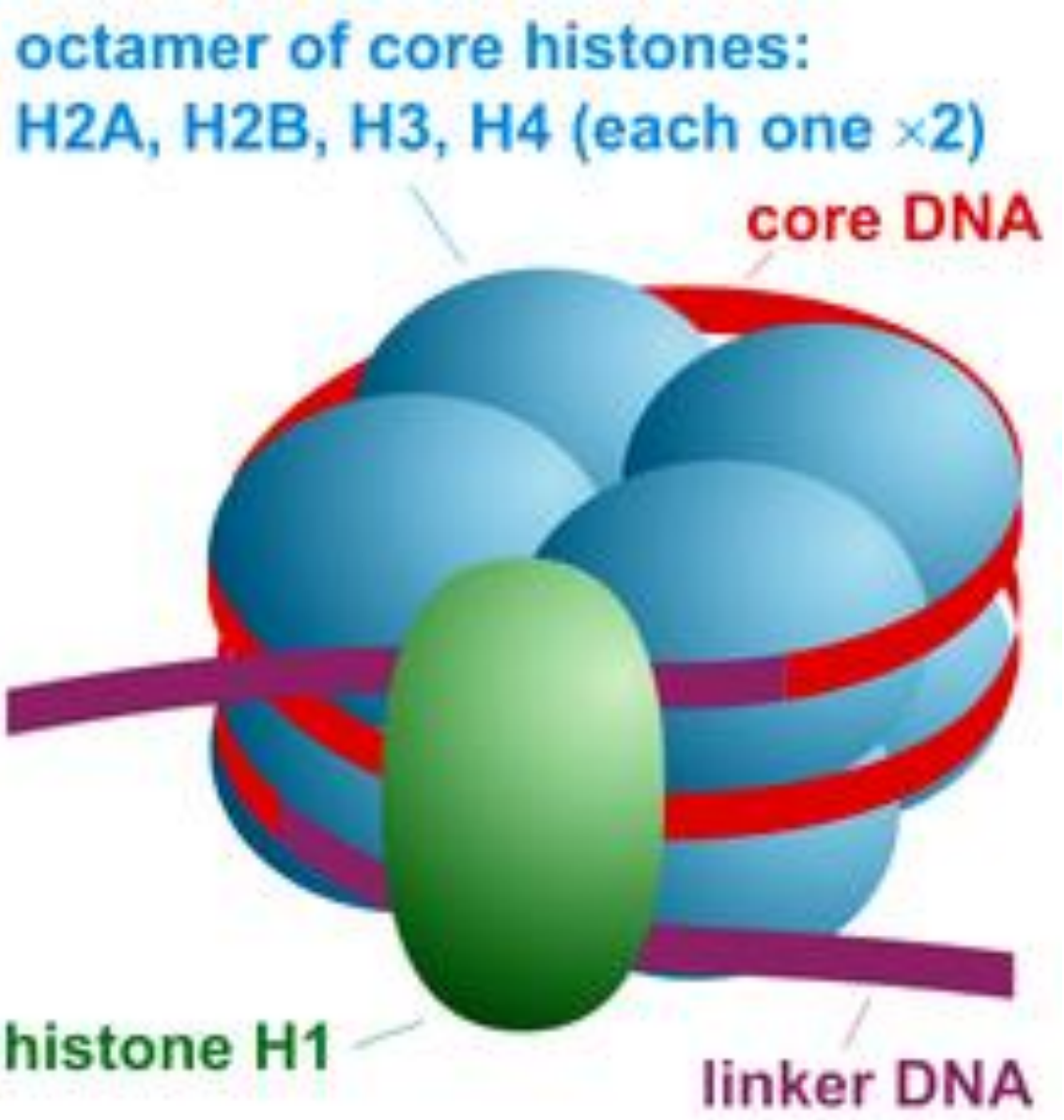
aminoacyl tRNA synthetase

Transfer RNA (tRNA)

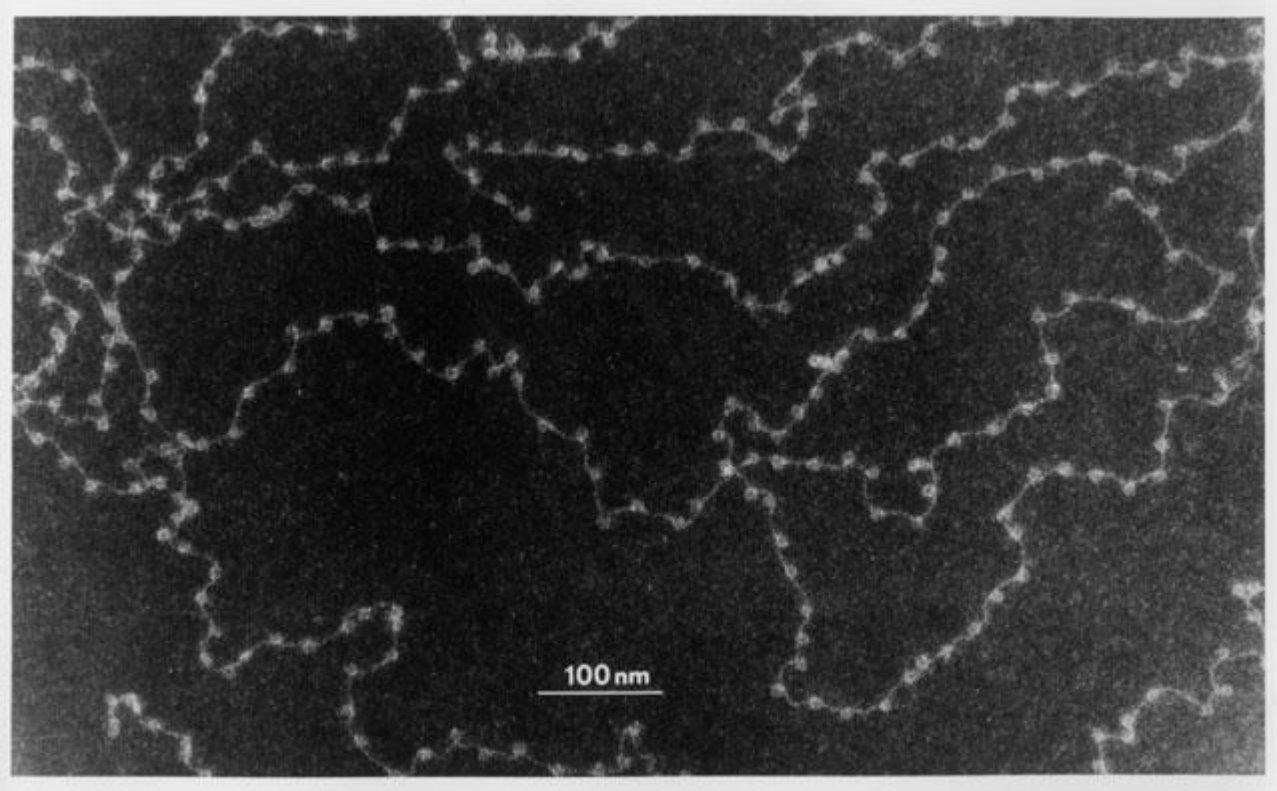
Produced from DNA by RNA polymerase III

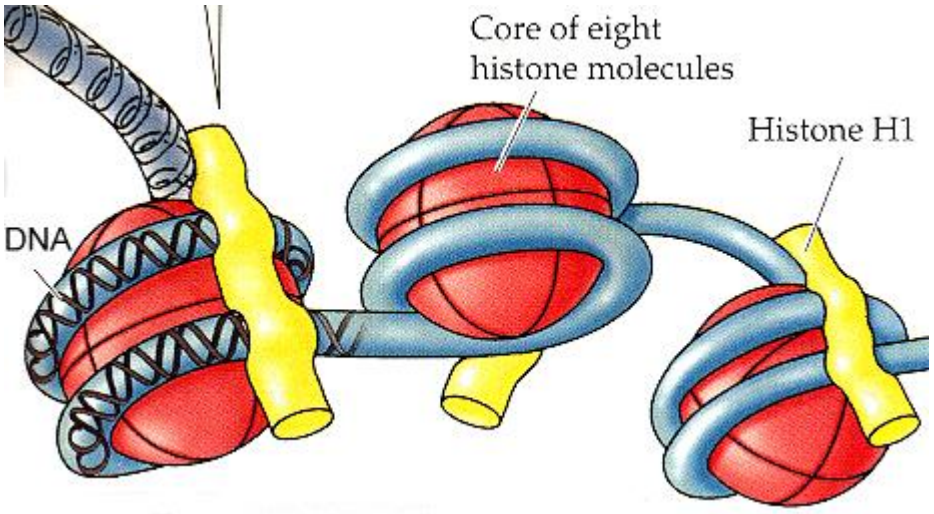
tRNA transfers activated amino acids to the ribosome-mRNA complex. Here amino acids are incorporated into forming protein.

NUCLEOSOME

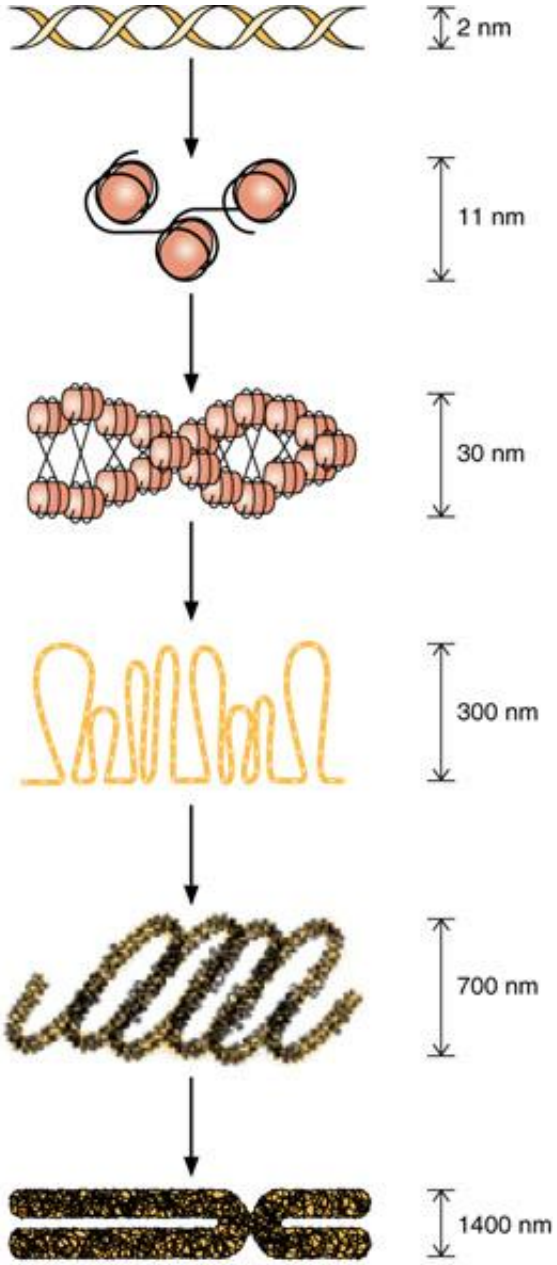

octamer of core histones:
H2A, H2B, H3, H4 (each one ×2)
core DNA
histone H1
linker DNA

"beads on a string" structure (euchromatin).





The order of chromatin packing



2-nm DNA double helix

„Beads on a string”

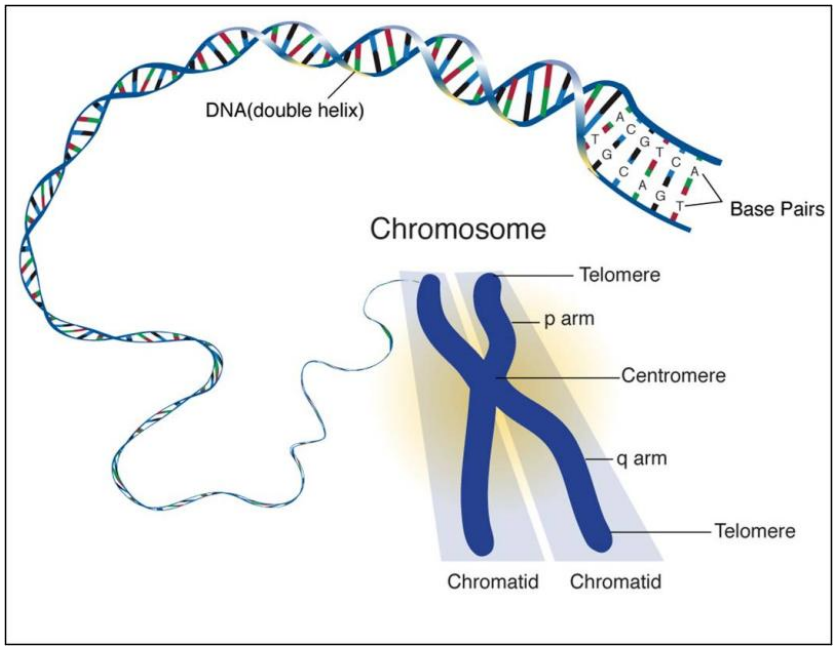
Association of DNA with octamer of histones; formation of 11nm

And with H1 - 30 nm fibers of chromatin

Further condensation, formation of 300 and 700 nm filaments

Maximal packing of DNA in metaphase **chromosome**

CHROMOSOMES - are maximally condensed in metaphase.

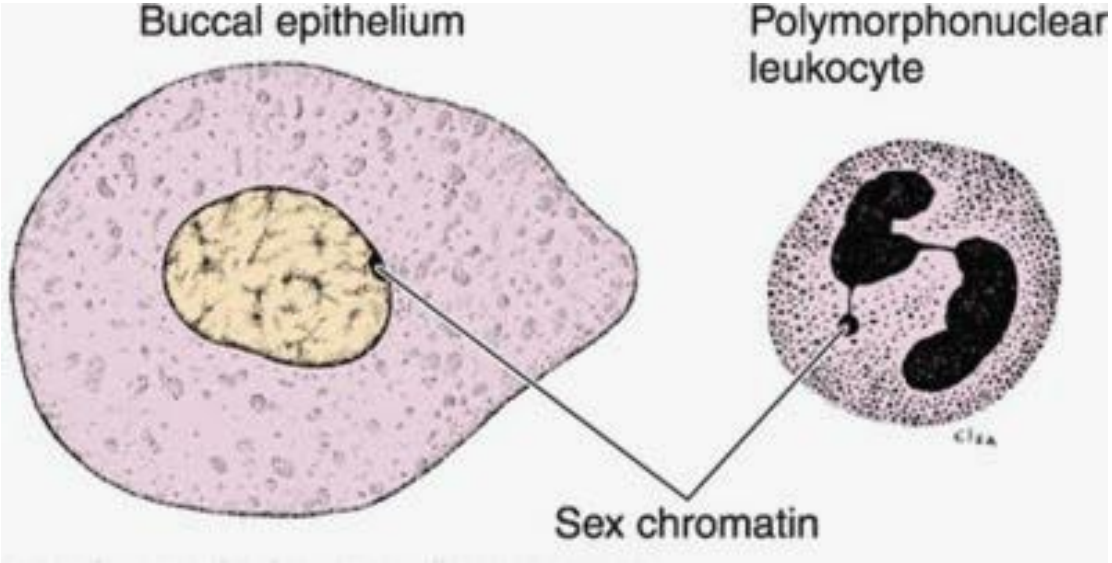


Human genom consists of 23 homologous pairs of chromosomes (maternal and paternal) – 22 autosomes and 1 pair of sex chromosomes.

Cells containing full set of chromosomes are diploid – **2n**. They have 23 pairs of chromosomes. These cells have also 2 copies of each gene – **2c**.

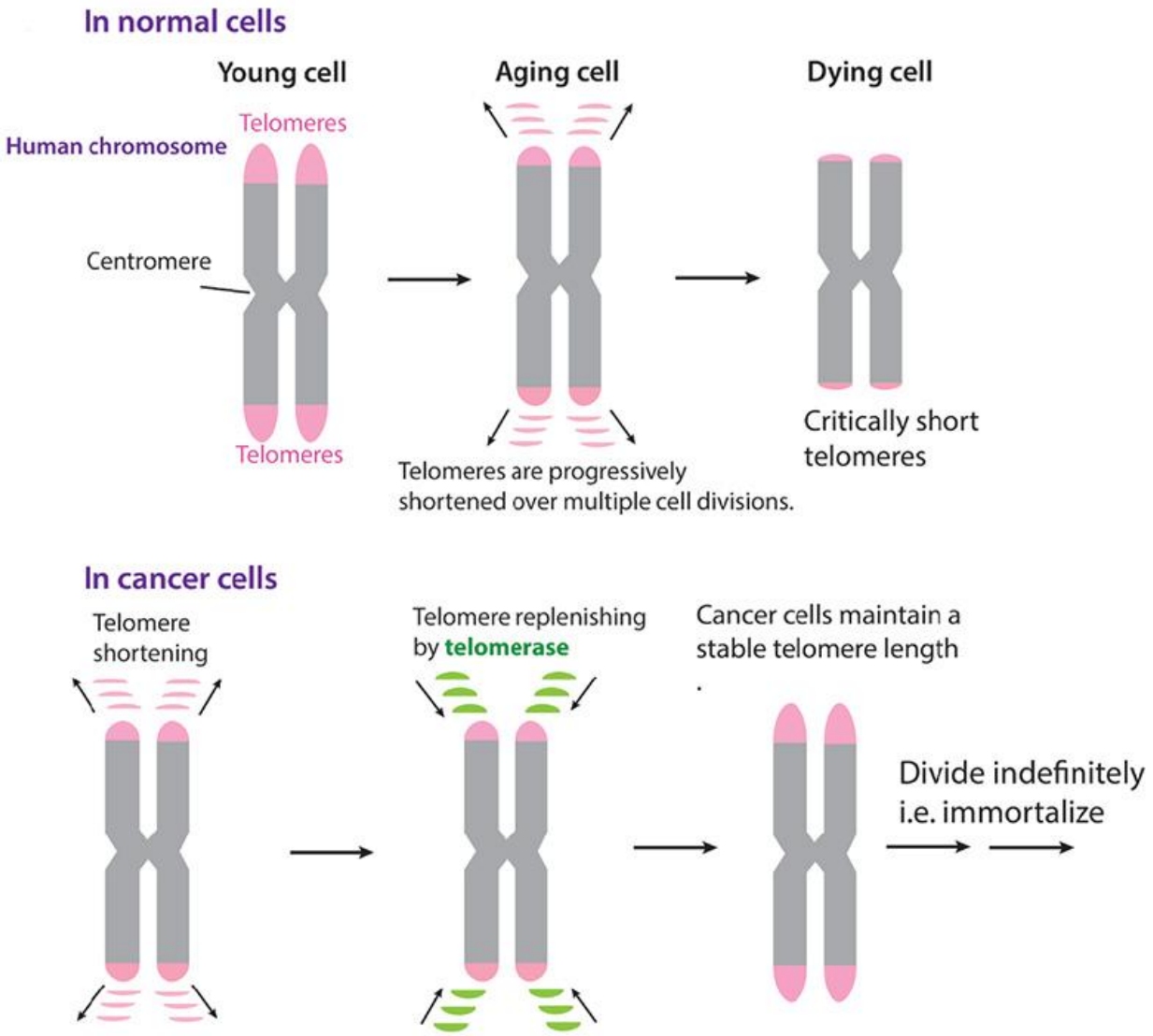
Gametes are haploid **1n**. They have only 1 copy of each gene – **1c**.

Sex chromatin in female epithelium (dense granule) and leukocyte (drumstick shape)



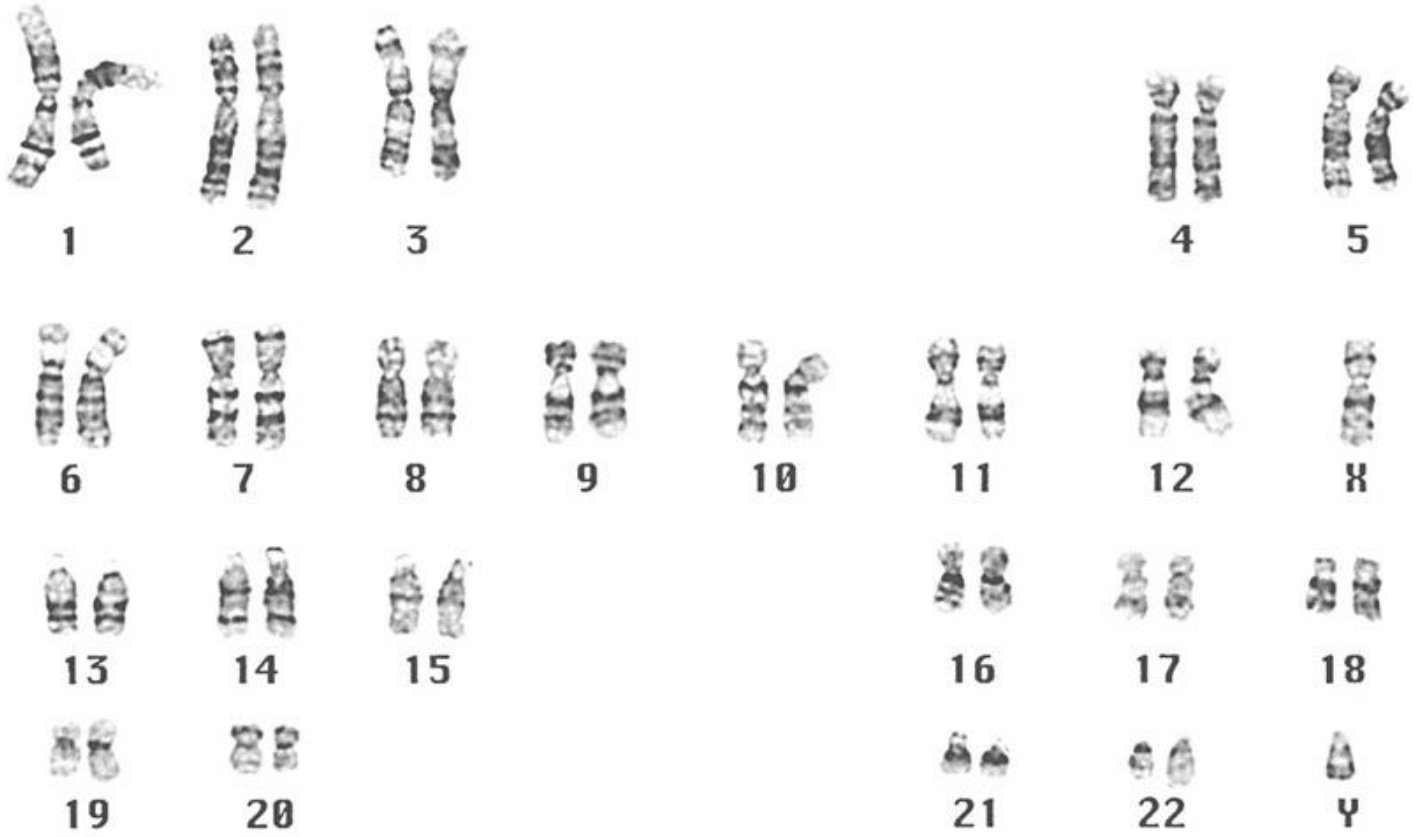
Only one of the two X chromosomes in female somatic cells is transcriptionally active. The inactive X chromosome remains inactive throughout the life of that individual.

Telomeres and telomerase



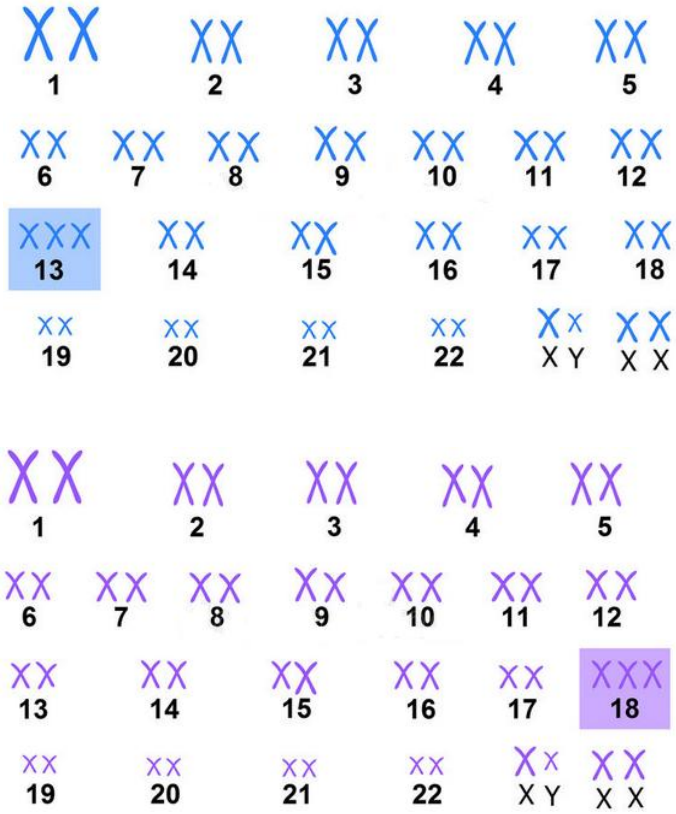
Human karyotype - A karyotype is the number and appearance of chromosomes in the nucleus of a cell.

Karyotype is used to study chromosomal aberrations



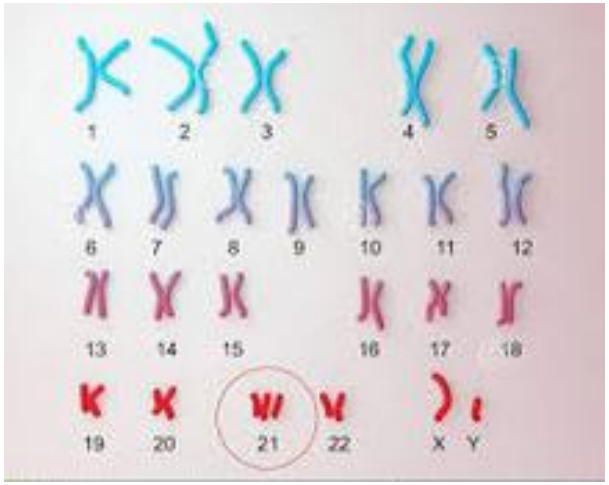
Banding is obtained after special staining, e.g. with Giemsa stain (adenine-thymine-rich regions of chromosomes).

Chromosomal anomalies within autosomes



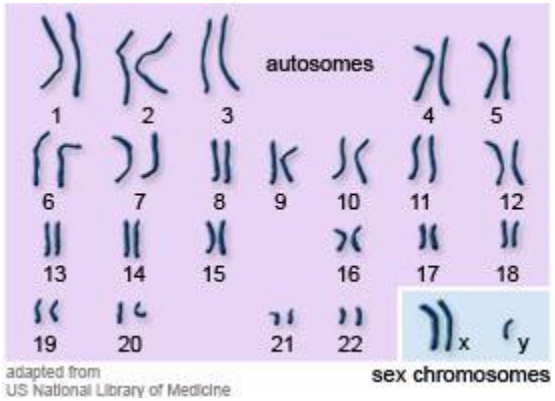
Patau syndrome - mental retardation, numerous malformations, cardiopathy and kidney abnormalities. Reduction of muscle tension, small hands, ears,

Edwards syndrome – Multi-organ defects. Heart defects. Other characteristics include a small head, a small jaw, clenched fists with overlapping fingers, and severe intellectual disability.

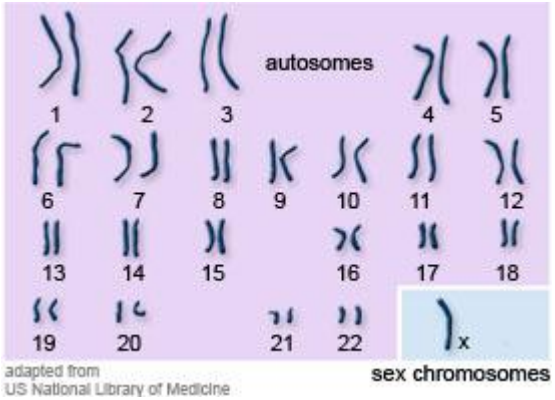


Down syndrome - growth retardation, characteristic facial features and mild to moderate intellectual disability

Chromosomal anomalies within sex chromosomes

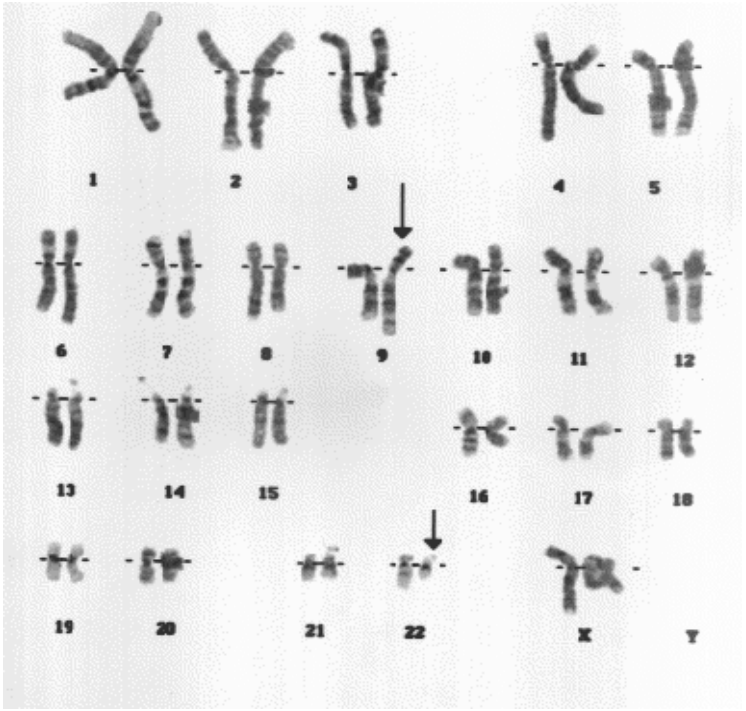


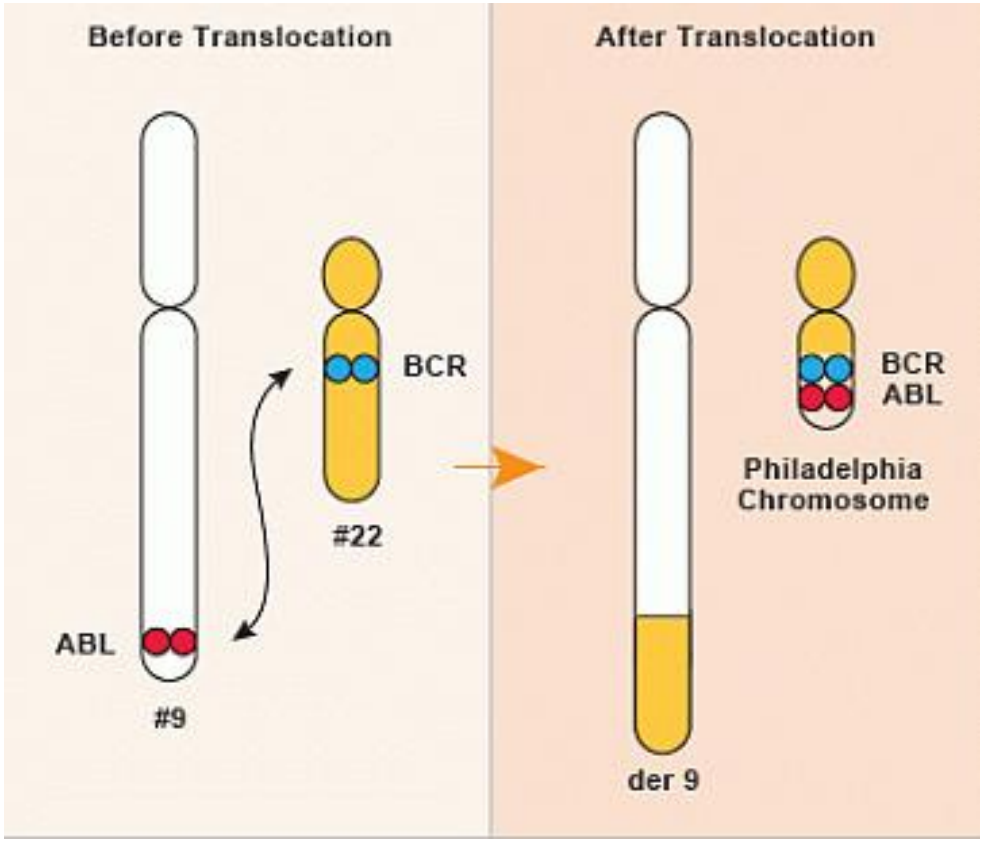
Klinefelter syndrome - Two X chromosomes and one Y chromosome (47,XXY). Many men with an extra X chromosome have no obvious symptoms and may never know they have this syndrome. The most common symptom is infertility.



Turner syndrome - A woman inherits only one X chromosome and does not have a second sex chromosome (45,X).

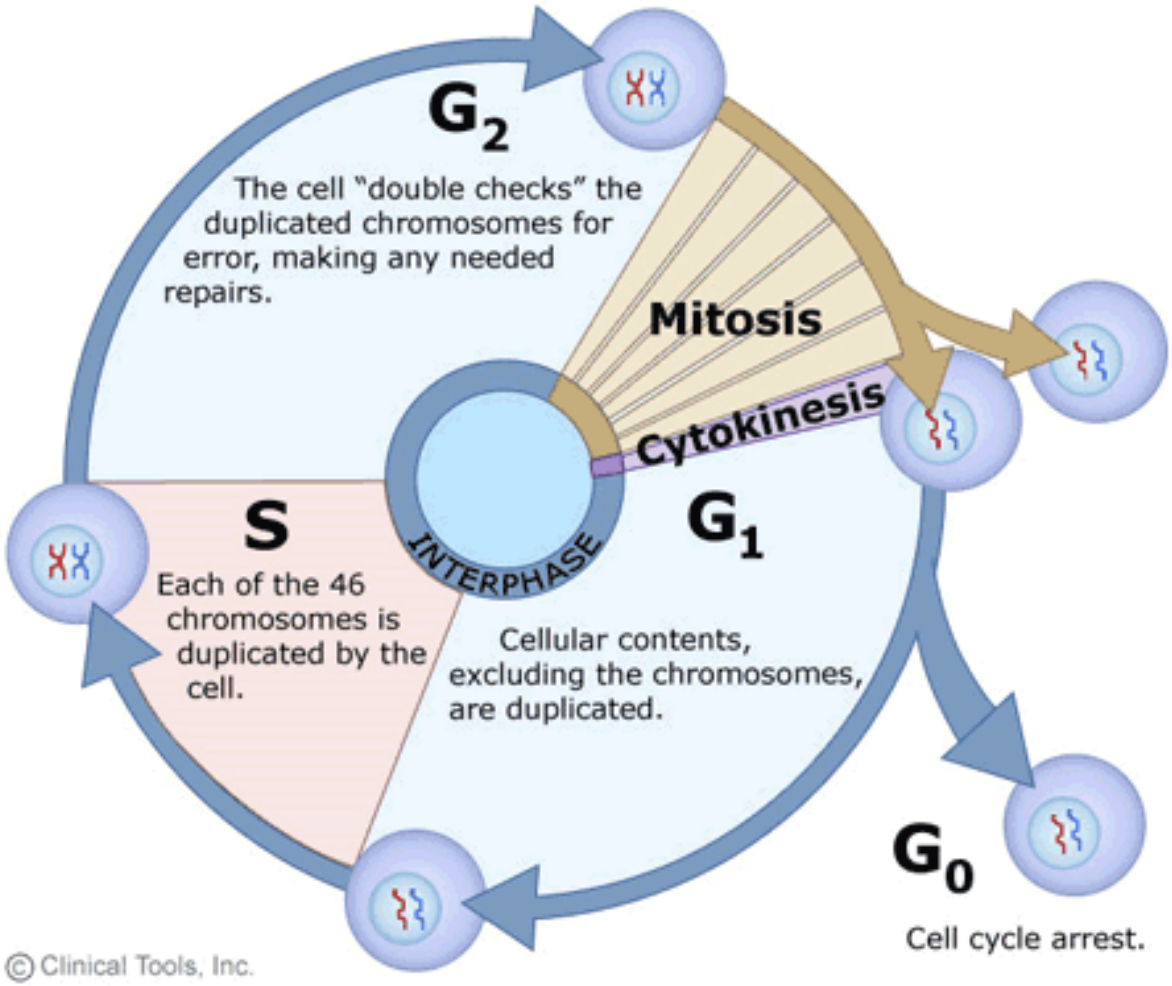
Philadelphia chromosome - is a specific chromosomal abnormality that is associated with chronic myelogenous leukemia (acute lymphoblastic leukemia and acute myelogenous leukemia).



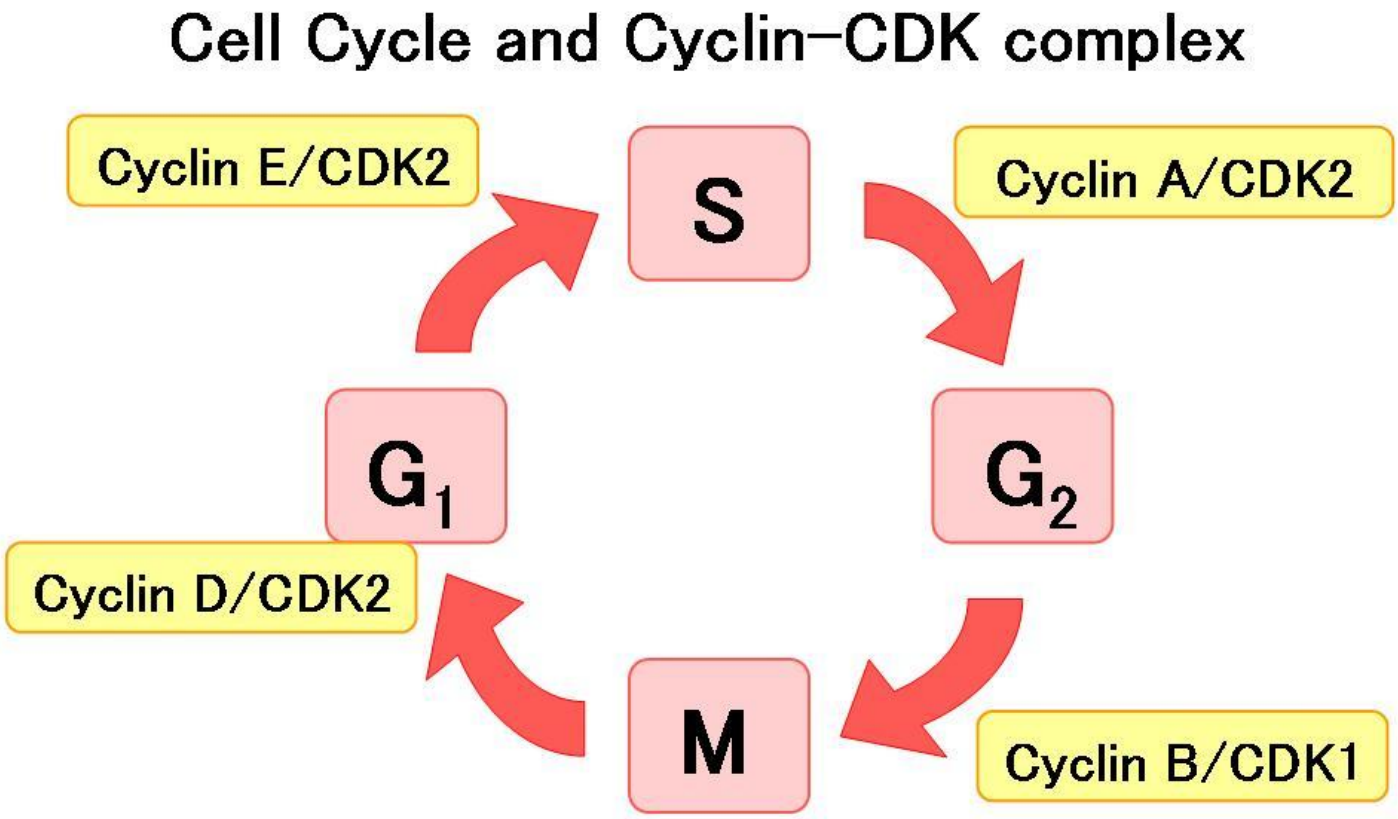


The four phases of the cell cycle

The cell cycle is divided into two major events: **interphase**, a long period of time, and **mitosis**, a shorter period of time. Interphase is subdivided into three phases.

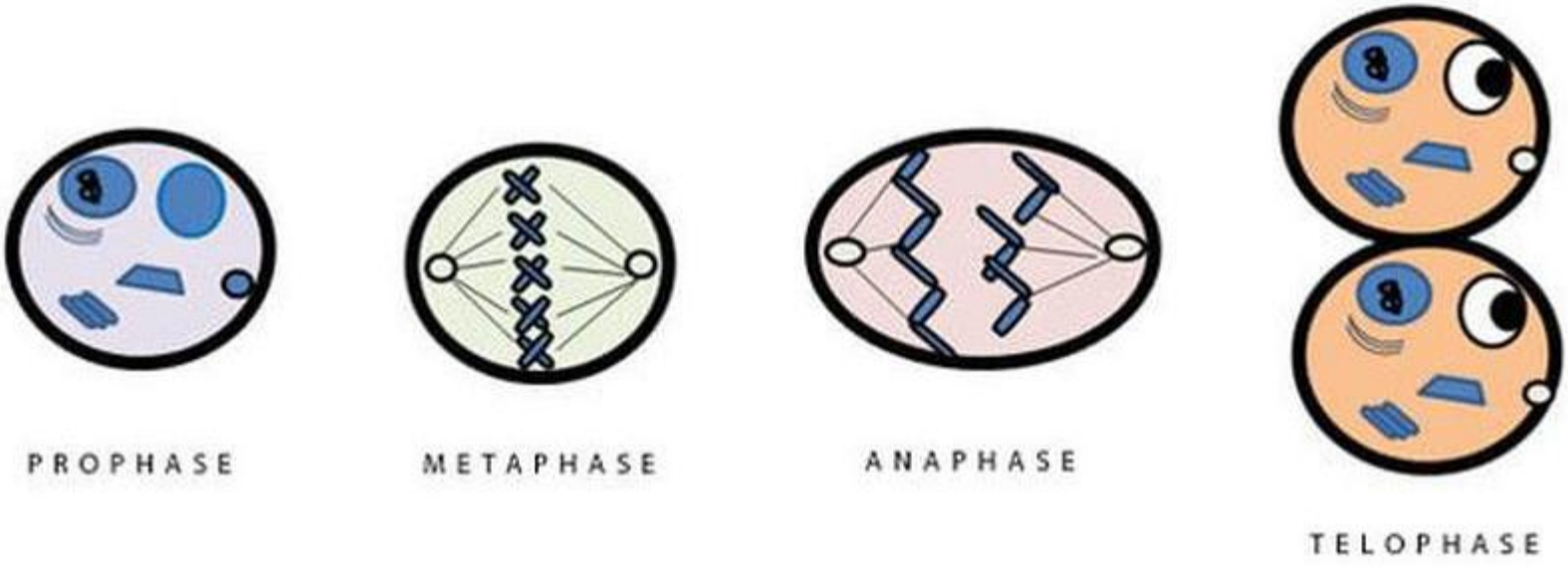


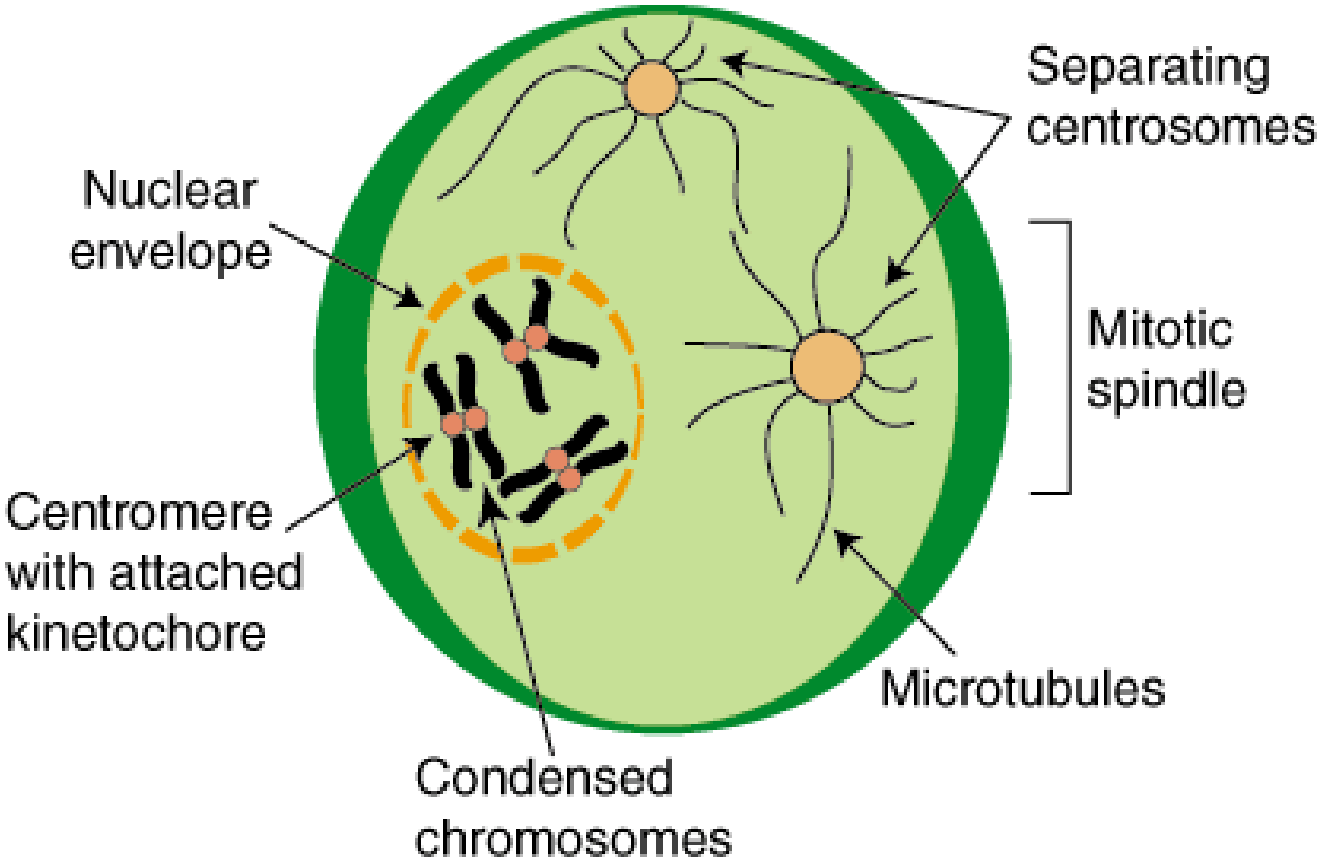
Two key classes of regulatory molecules, **cyclins** and **cyclin-dependent kinases (CDKs),** determine a cell's progress through the cell cycle.



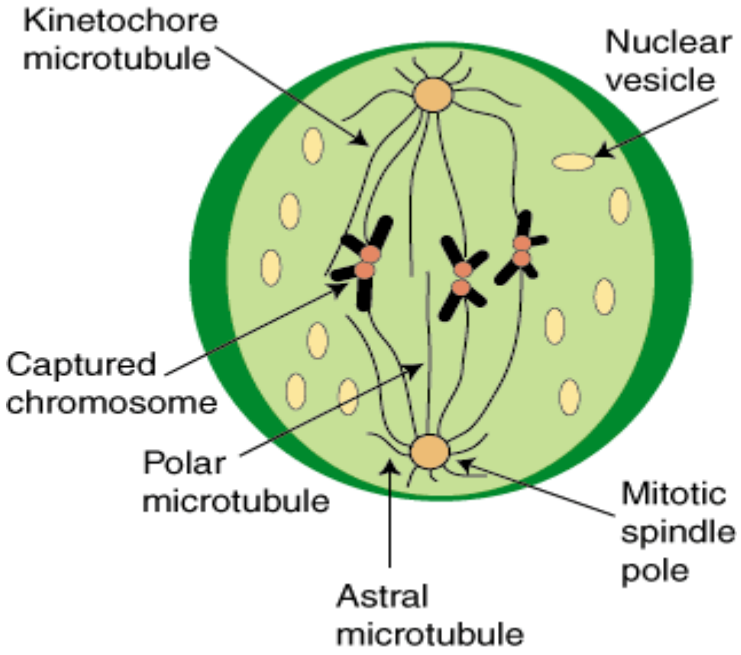
MITOSIS

- is the process of cell division of somatic cells that results in the formation of two identical daughter cells. Mitosis is divided into a **karyokinesis** (nucleus division) and **cytokinesis** (cytoplasm division). Karyokinesis is subdivided into **prophase, prometaphase, metaphase, anaphase and telophase**.

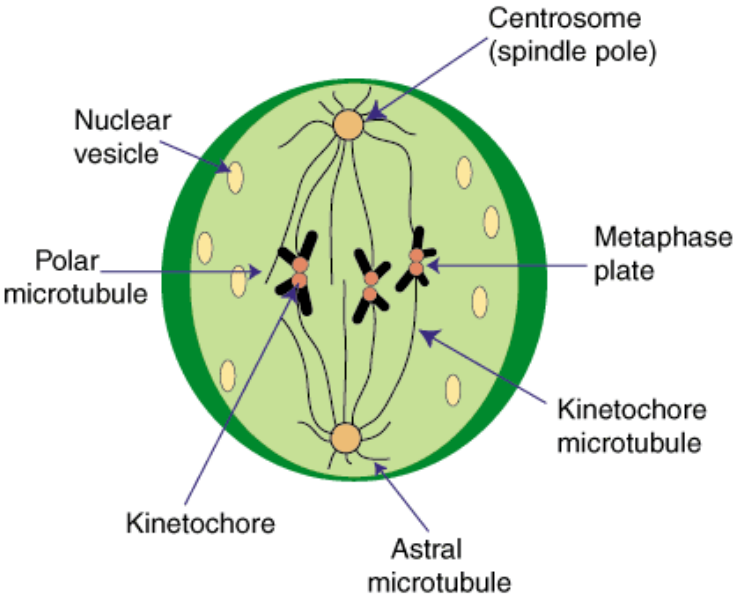




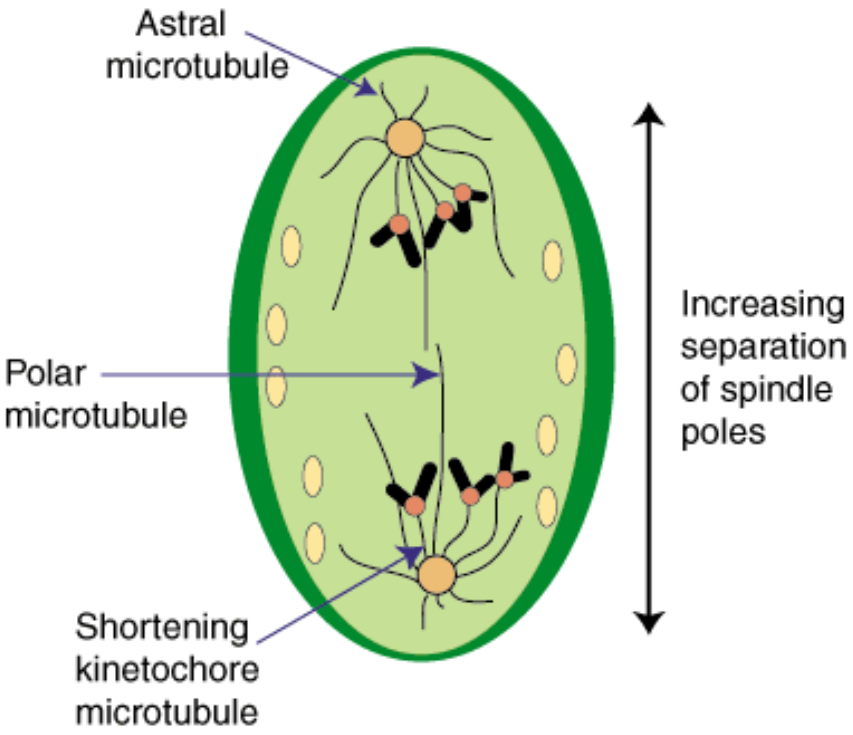
Prophase – the chromosomes condense (two chromatids joined in centromere), the nucleolus disappears.



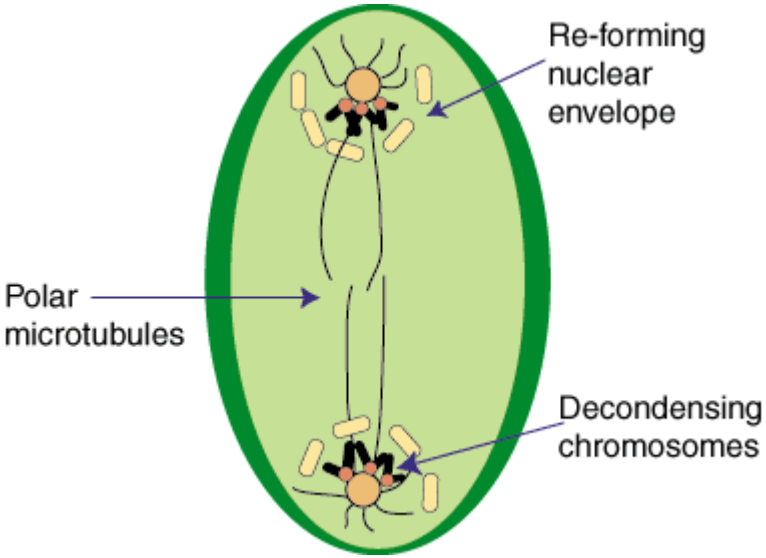
Prometaphase - disappearance of the envelope

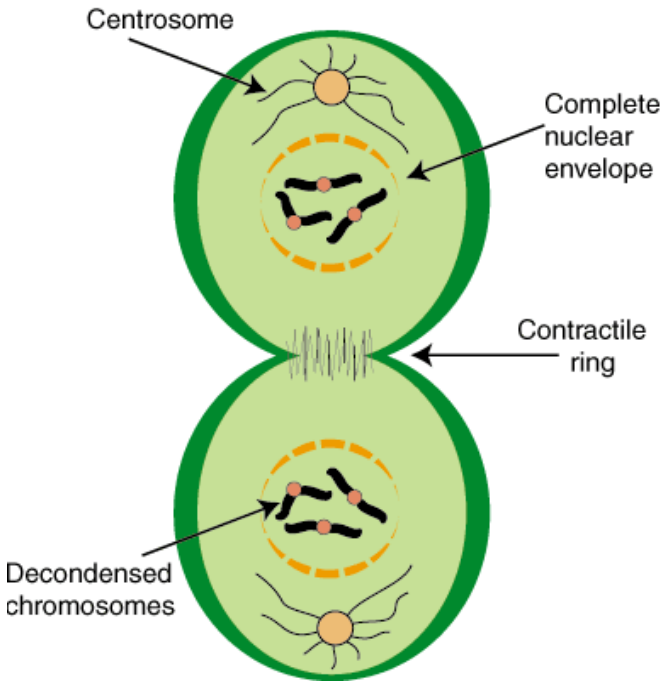


Metaphase - chromosomes are lined up at the equator of the mitotic spindle – metaphase plate



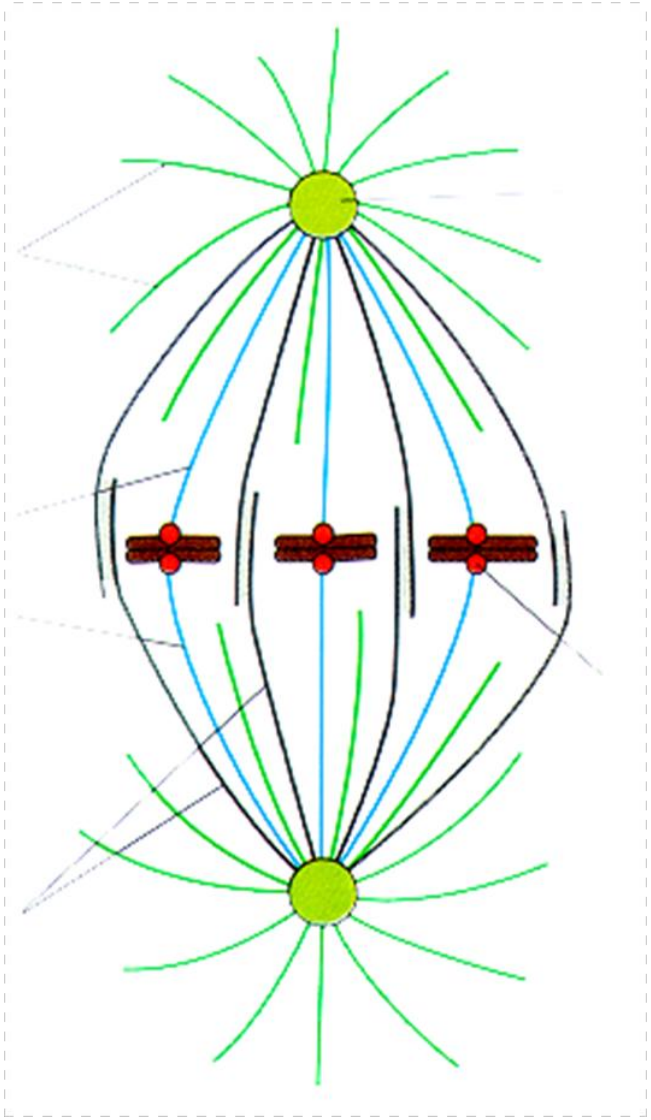
Anaphase - sister chromatids migrate to opposite poles of the cell. In late anaphase a cleavage furrow begins to form.

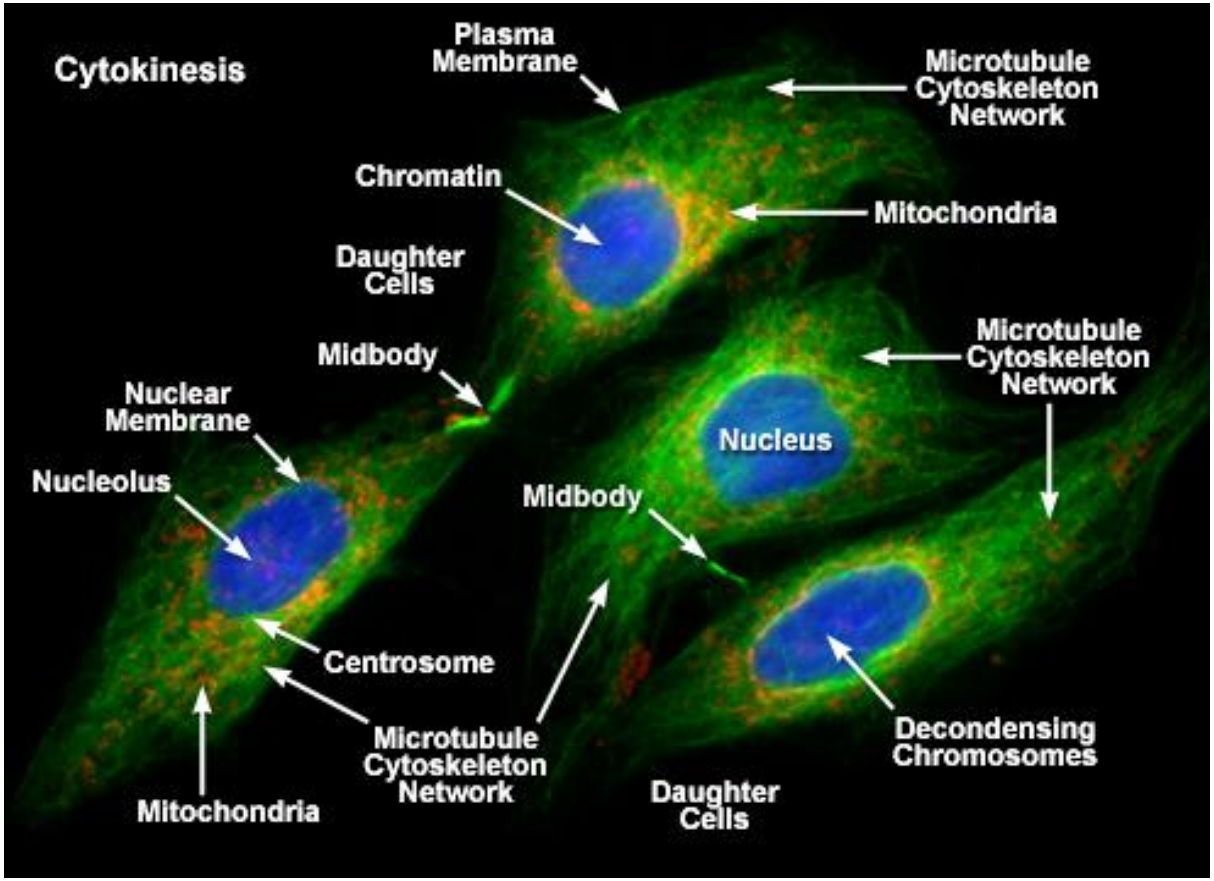




Telophase -each set of chromosomes is in its respective pole, nucleolus is reconstituted. Cytokinesis occurs

Microtubules in mitosis





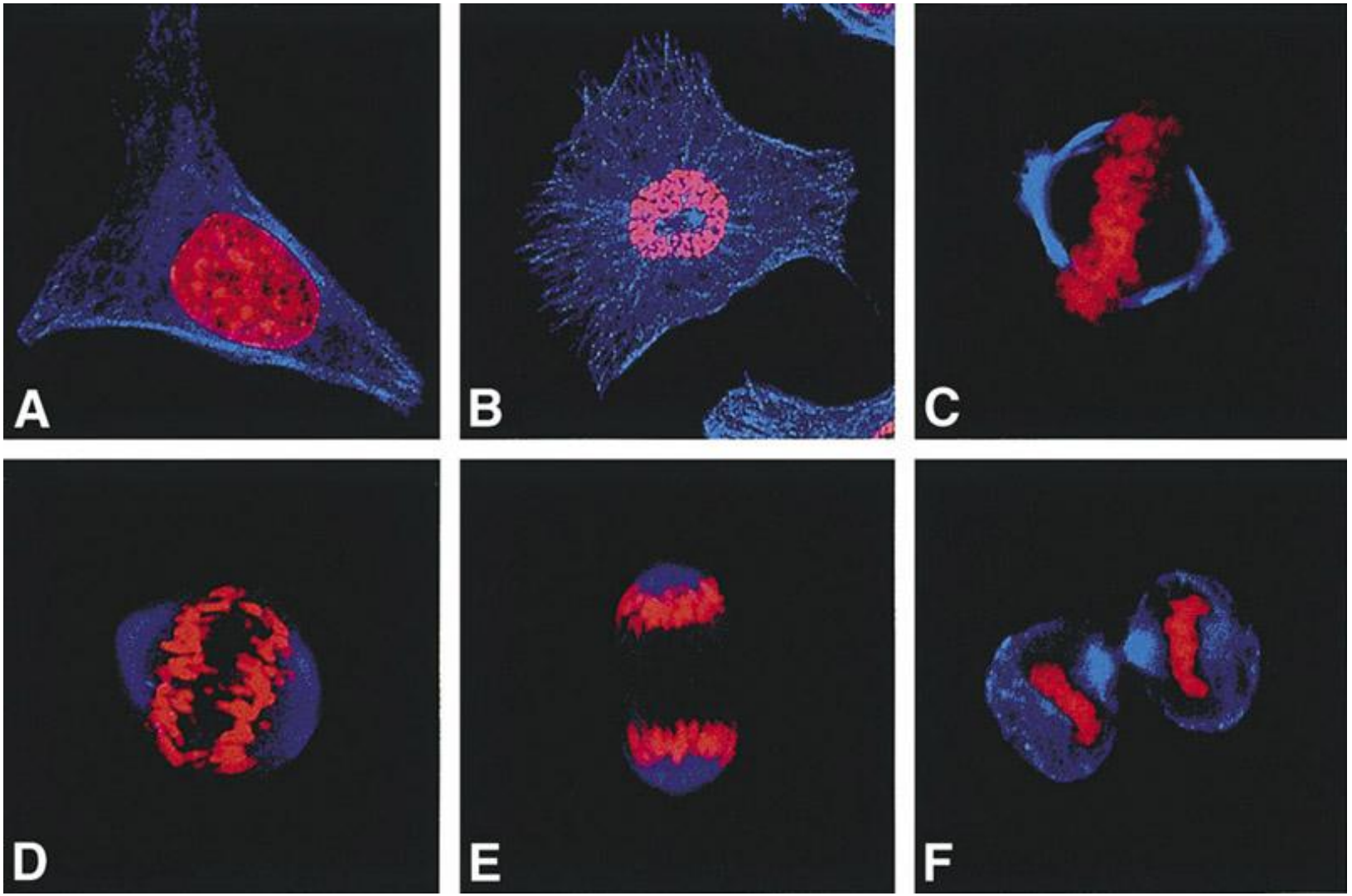
CYTOKINESIS

in fluorescent microscope

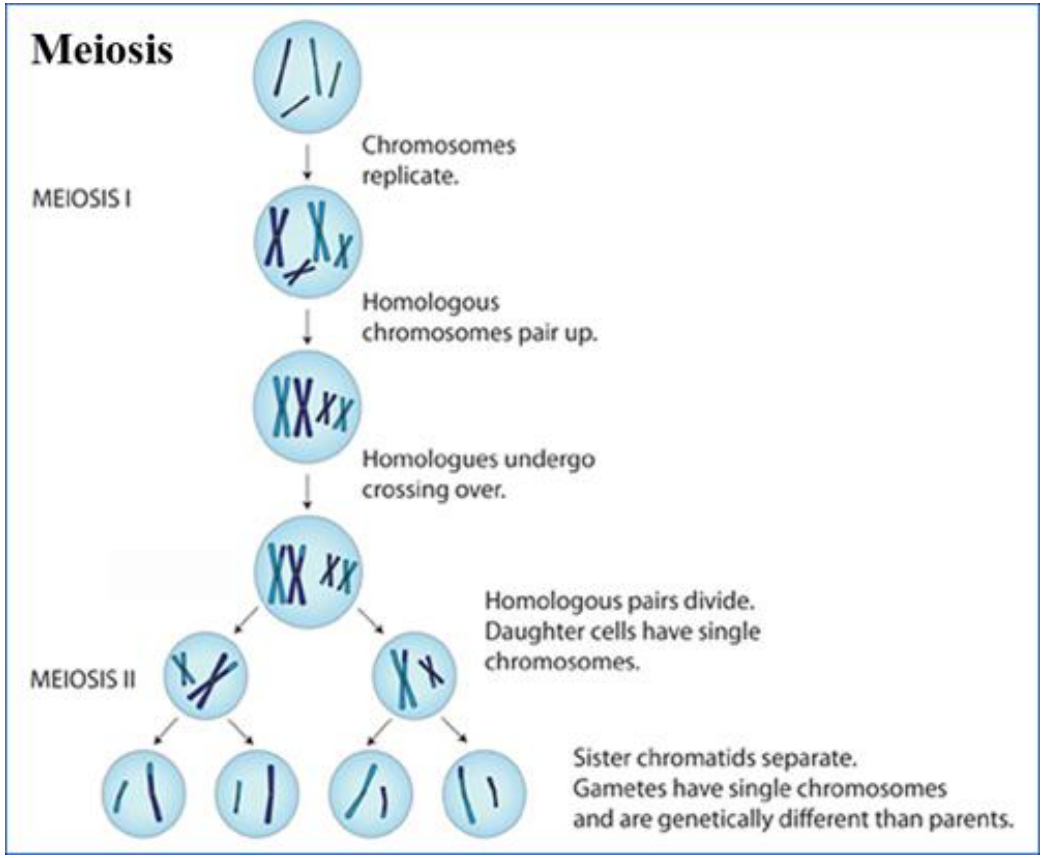
Division of cytoplasm into two equal parts

- contractile ring composed of actin and myosin filaments

Confocal laser scanning microscope – phases of mitosis. DNA is red and microtubules blue



MEIOSIS - Type of cell division resulting in the formation of gametes (**spermatozoa or ova**) whose chromosome number has been **reduced to the haploid 1n number** and **recombination of genes** occurs

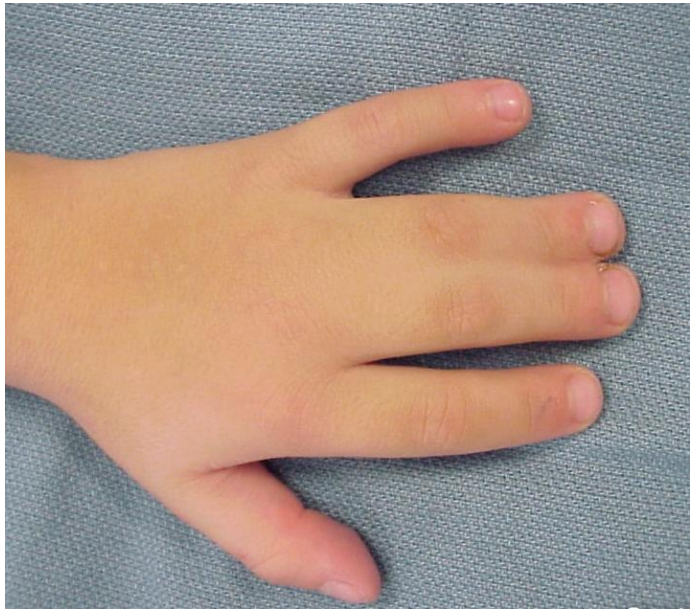


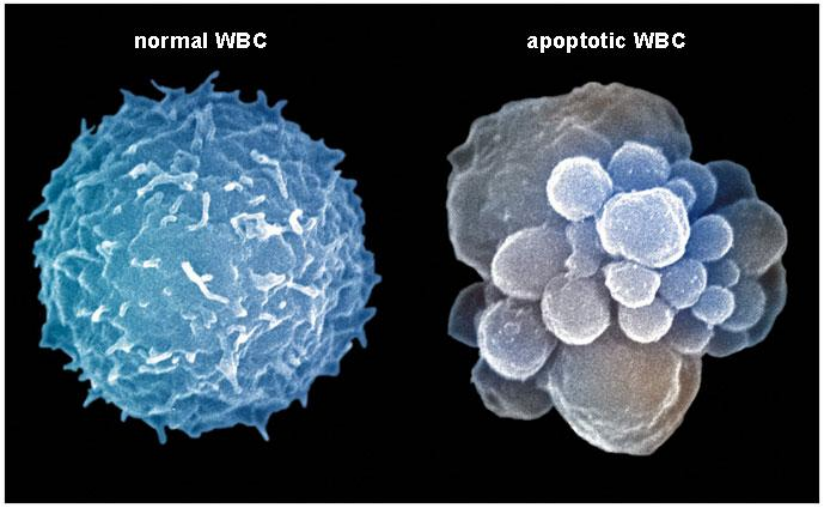
Meiosis is divided into:

- **meiosis I** – reductional division
- **meiosis II** – equatorial division

APOPTOSIS

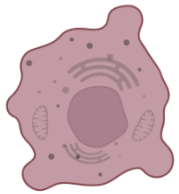
the process of programmed cell death in multicellular organisms





Necrosis

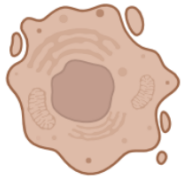
Small blebs form and and the structure of the nucleus changes



The blebs fuse and become larger, while no organelles are located in the blebs

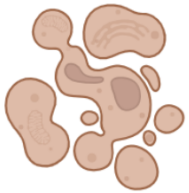
Cell lyses and releases content, while the organelles are not functional

Apoptosis

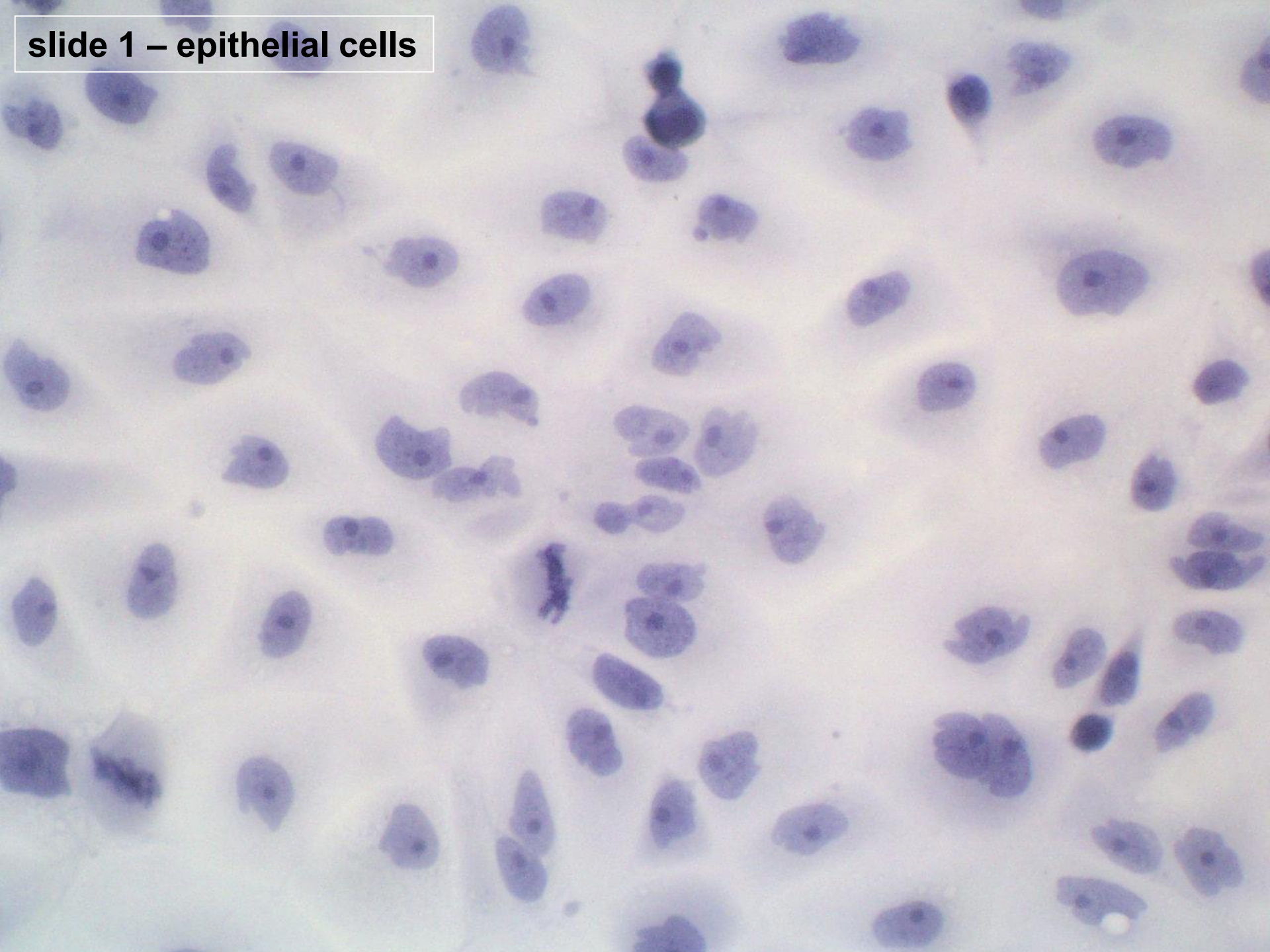


Small blebs form

The nucleus, DNA, and organelles break off within blebs



The cell breaks into several apoptotic bodies and the organelles are still functional


slide 1 – epithelial cells