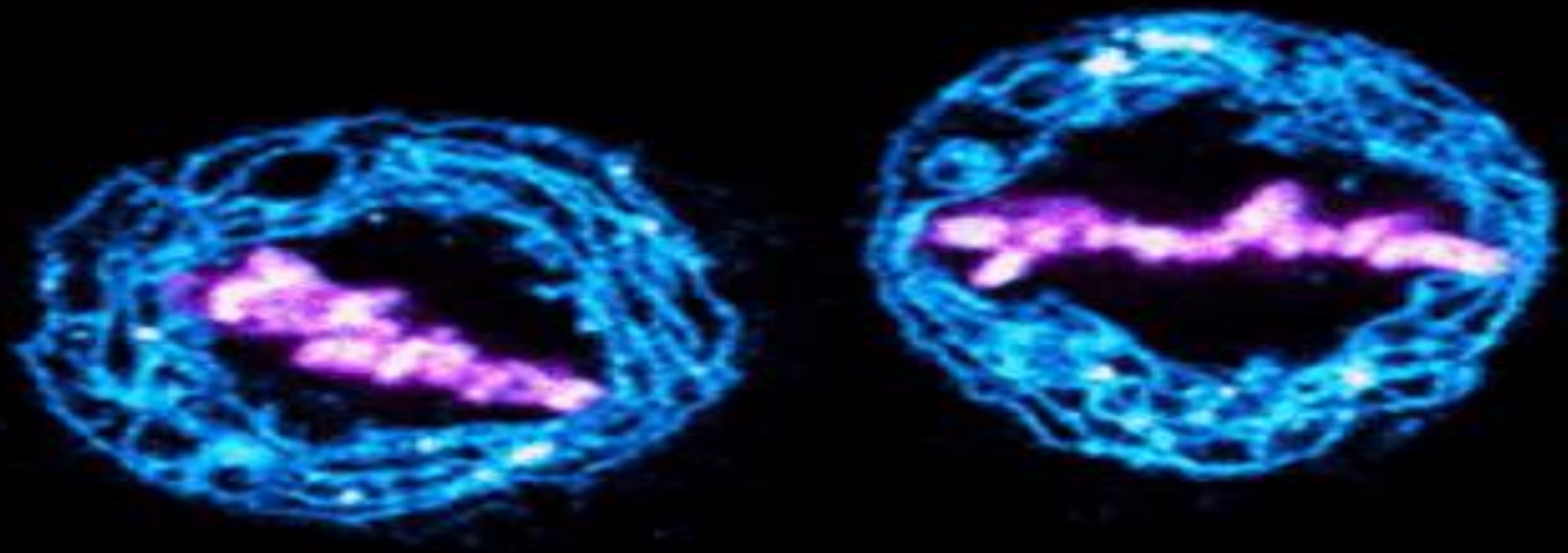
The Cell as a Unit of Health and Disease and Cell Cycle



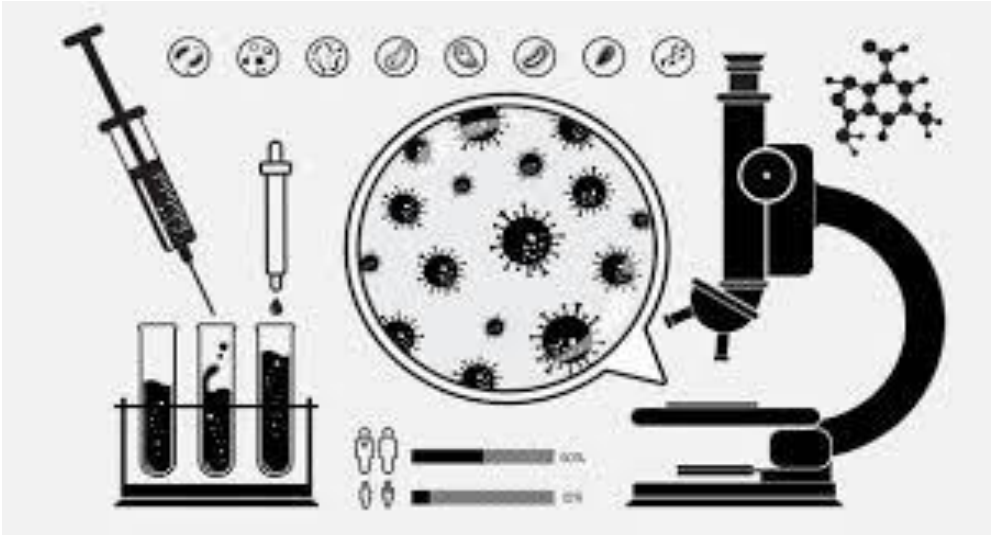
Objectives

At the end of the session student's should be able to:

- Understand the Cell as a Functional Unit and explain the role of the cell as the basic structural and functional unit of life
- Explain the Cell Cycle and Its Regulation – Outline the phases of the cell cycle, including key regulatory mechanisms controlling cell growth and division.
- Relate the Cell Cycle to Disease Processes – Understand how dysregulation of the cell cycle leads to diseases such as cancer and other proliferative disorders.

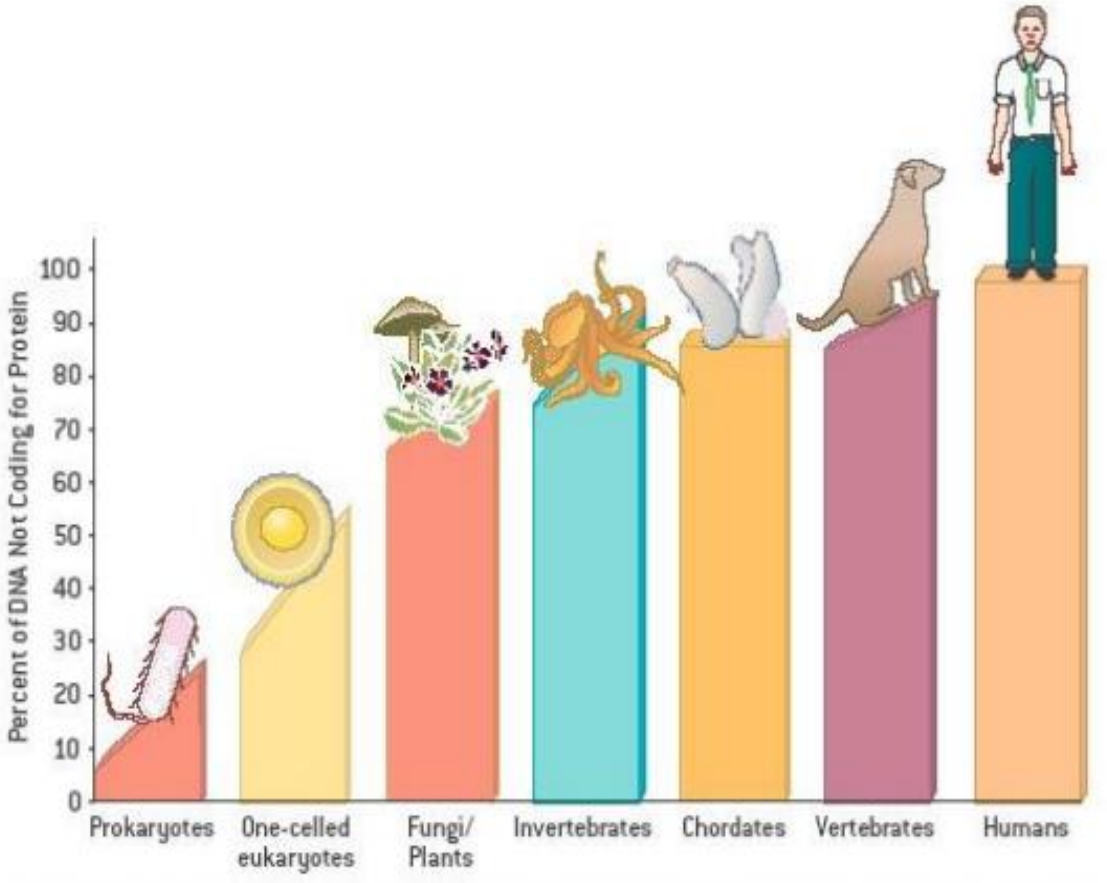
Pathology

- Pathology means the study of suffering
- Greek pathos = suffering, logos = study
- Term pathology is invoked to represent the study of disease

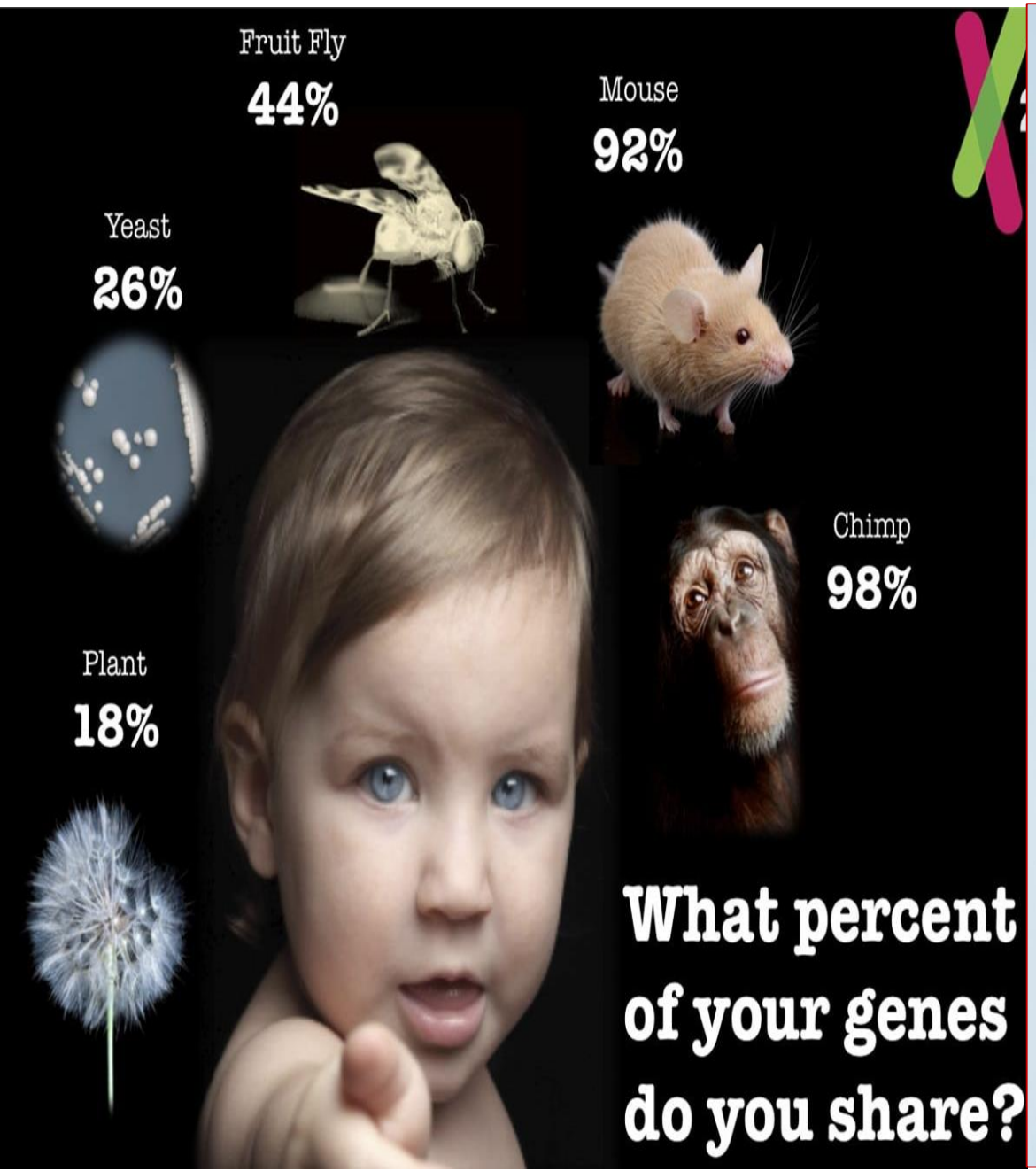


??? Dark part of Genome

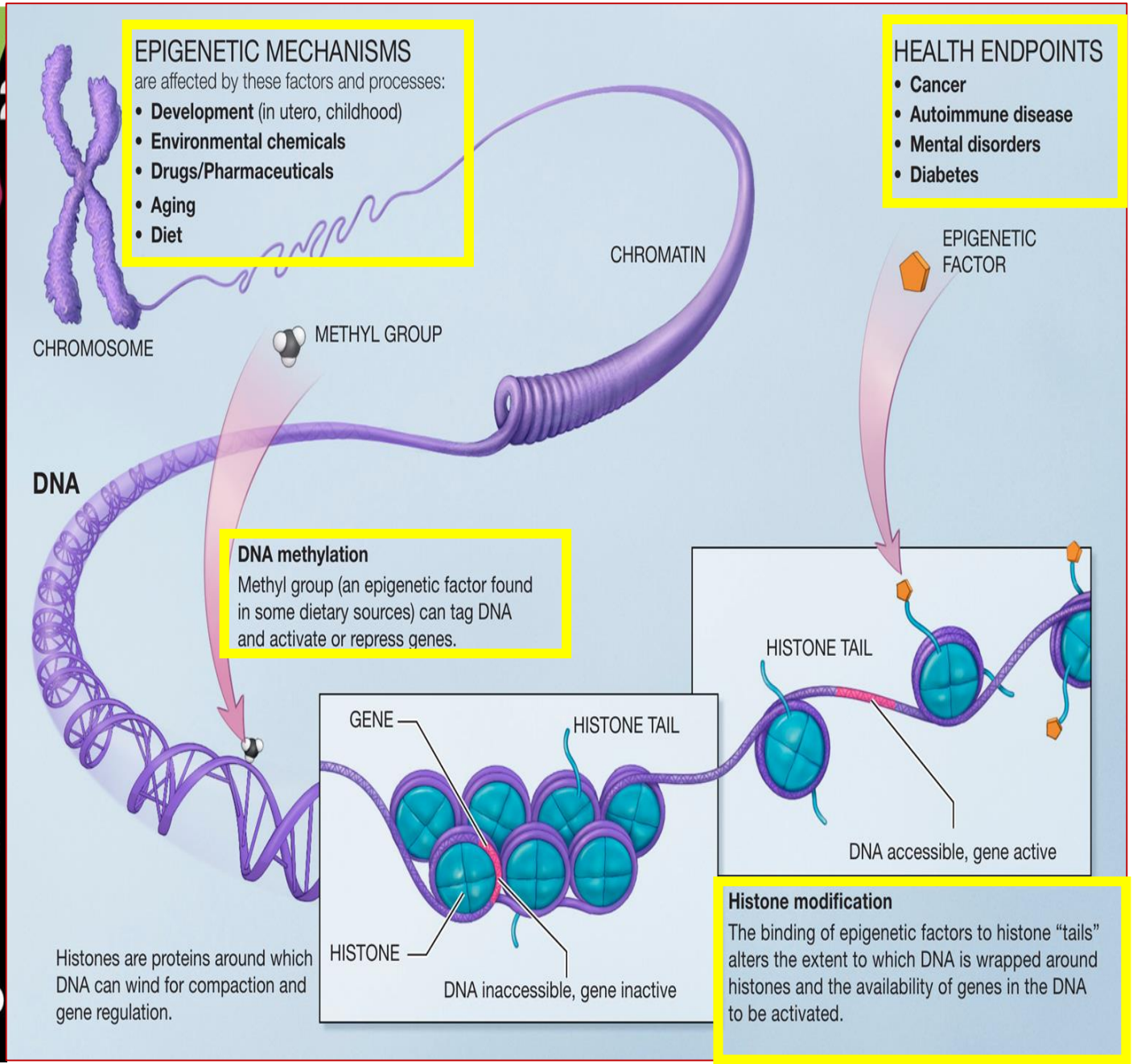
- The human genome contains roughly 3.2 billion DNA base pairs
- Only 20,000 protein-encoding genes, comprising only about 1.5% of the genome
- Regulate the decoding process, or expression, of protein-making genes.



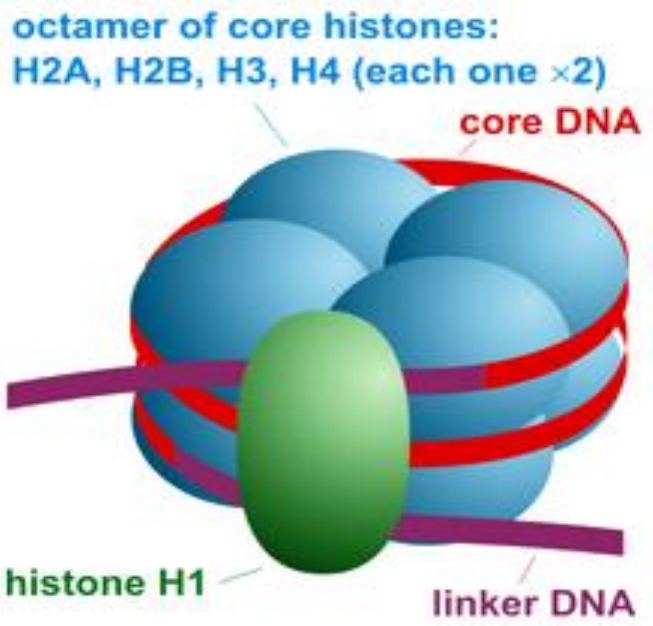
We are 99.9% same????



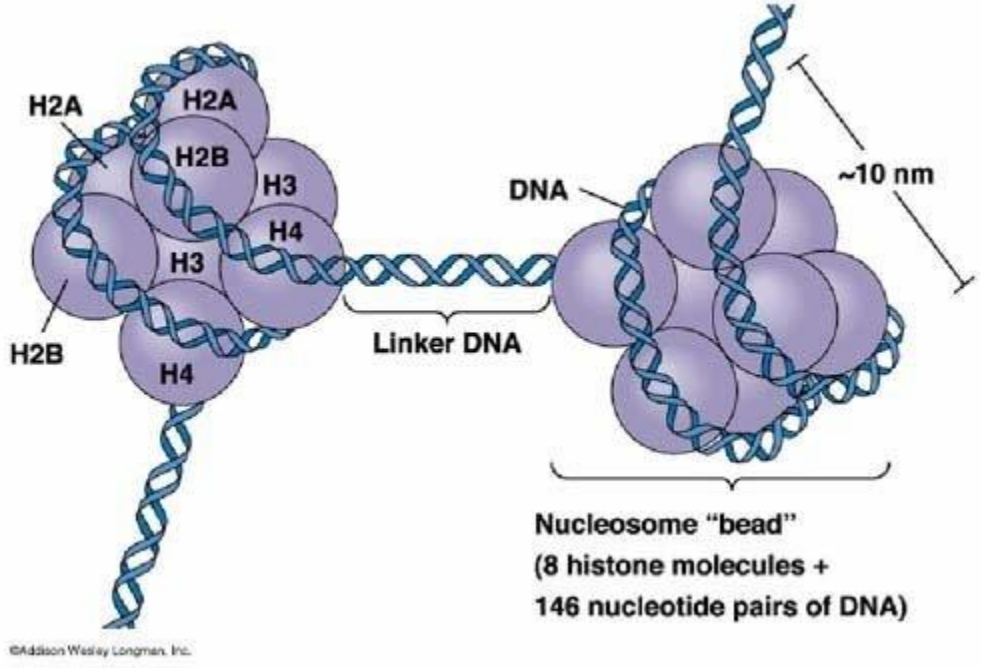
Epigenetics



Histone Organization

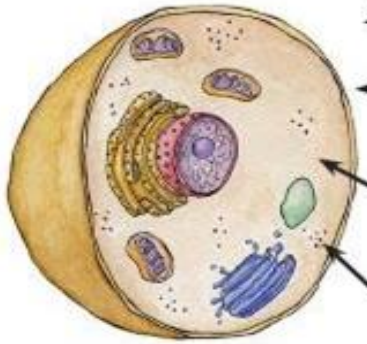


- Around 70 different histone modifications (Histone marks) are present
- Histone marks are reversed by “chromatin erasers.”
- These “marks” expose or obscure gene regulatory elements
- Proteins “chromatin readers,” binds to the histones bearing particular marks and thereby regulate gene expression



- ➢ Histone methylation (lysine and arginine)
- ➢ Histone acetylation (lysine)
- ➢ Histone phosphorylation (Serine)
- ➢ DNA methylation

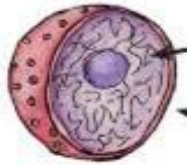
Animal Cell Organelles



1. Each cell has a protective outer layer – the plasma membrane. The plasma membrane lets certain things into the cell that it needs, but keeps other things out. This is called semipermeable.

2. Inside the cell is a watery medium that everything floats in called cytoplasm. The cytoplasm contains all the working parts of the cell, the organelles.

3. Little grains floating around inside the cell are ribosomes, where proteins are made.



4. The nucleus has our DNA that contains all our genetic information. The DNA is found on structures in the nucleus called chromosomes There are 23 pairs (46 total) of chromosomes in each nucleus of each cell.

5. The nucleus is surrounded by a nuclear membrane, which controls what goes in and out.

6. Rough endoplasmic reticulum (rough ER) is a series of folded membrane pathways spotted with ribosomes. Together the ribosomes and the rough ER make new proteins and new membranes that the cell needs.

7. Smooth Endoplasmic Reticulum (smooth ER) has no ribosomes on it and forms containers called transport vesicles that are used to move things around inside the cell.

8. Golgi apparatus are made up of saccules that package up things to be transported around the cell or that need to leave the cell, like hormones.

9. Lysosomes are vesicles that have digestive enzymes inside them and break down the things that the cell doesn't need. They also kill bacteria that invades the body.

10. Vacuoles are membrane large membranous sacs for storing things. Vesicles are smaller sacs.

11. Mitochondria have a double membrane that folds in on itself forming little finger-like projections called cristae. Inside is a gel-like matrix with enzymes that break down sugars to make ATP, which is used by the cell as energy. These very important organelles contain their own DNA and ribosomes, reproduce by division and can even produce some of their own proteins.

EXTRACELLULAR MATRIX (ECM)

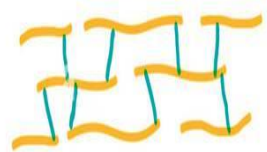
ECM is the material present outside the cell.
It is made up of different combinations of FIBRES and GROUND SUBSTANCE.
ECM helps in supporting cell, cell development,
motility, cell-cell interactions, cell division, etc.

I. ECM FIBRES
are long structures
secreted by fibroblasts.

Collagen

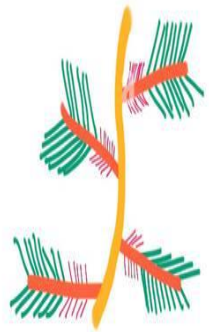
Reticular Fibre

Elastin

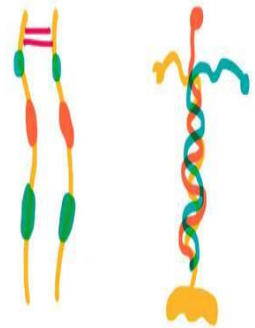


II. ECM GROUND SUBSTANCE
are long structures
secreted by fibroblasts.

Proteoglycan



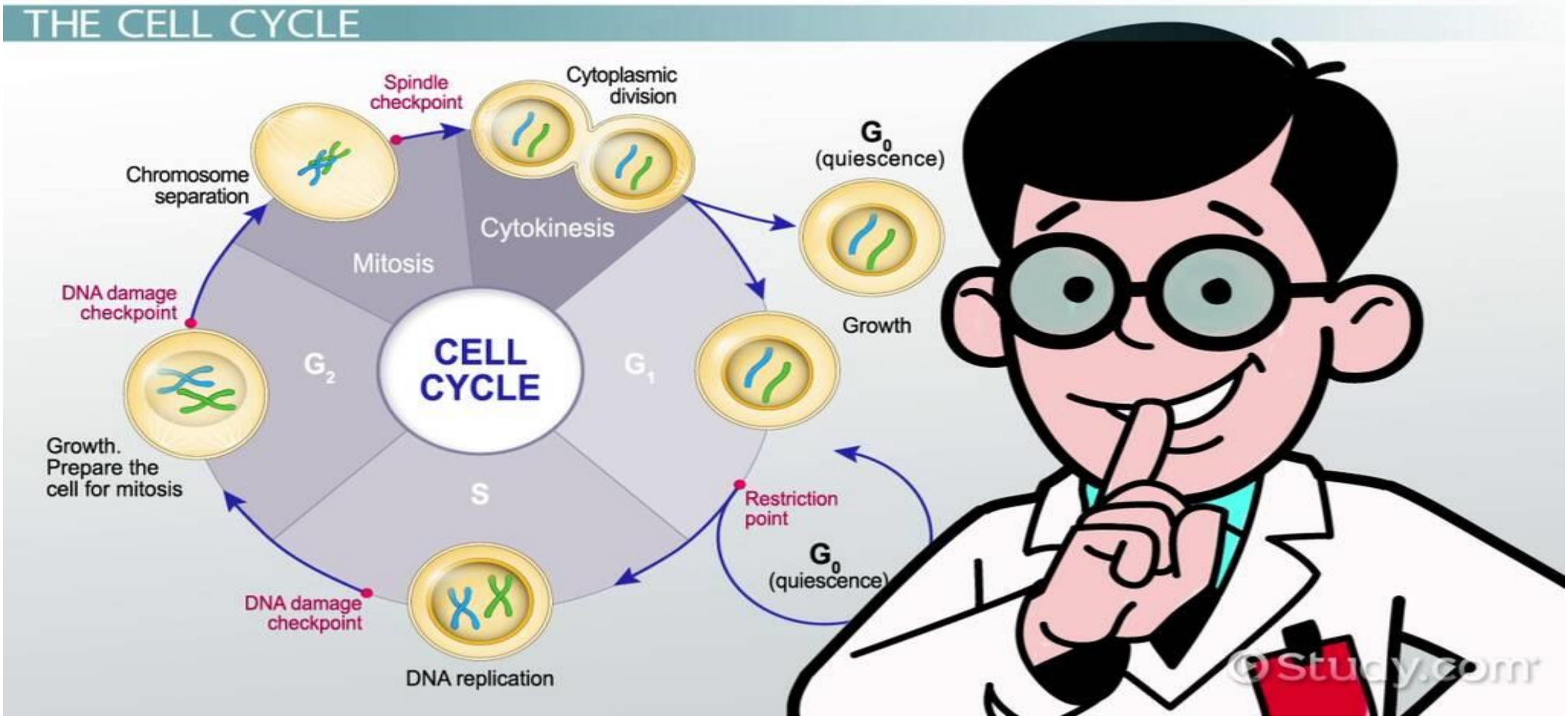
Multiadhesive
Glycoproteins



Cell Cycle

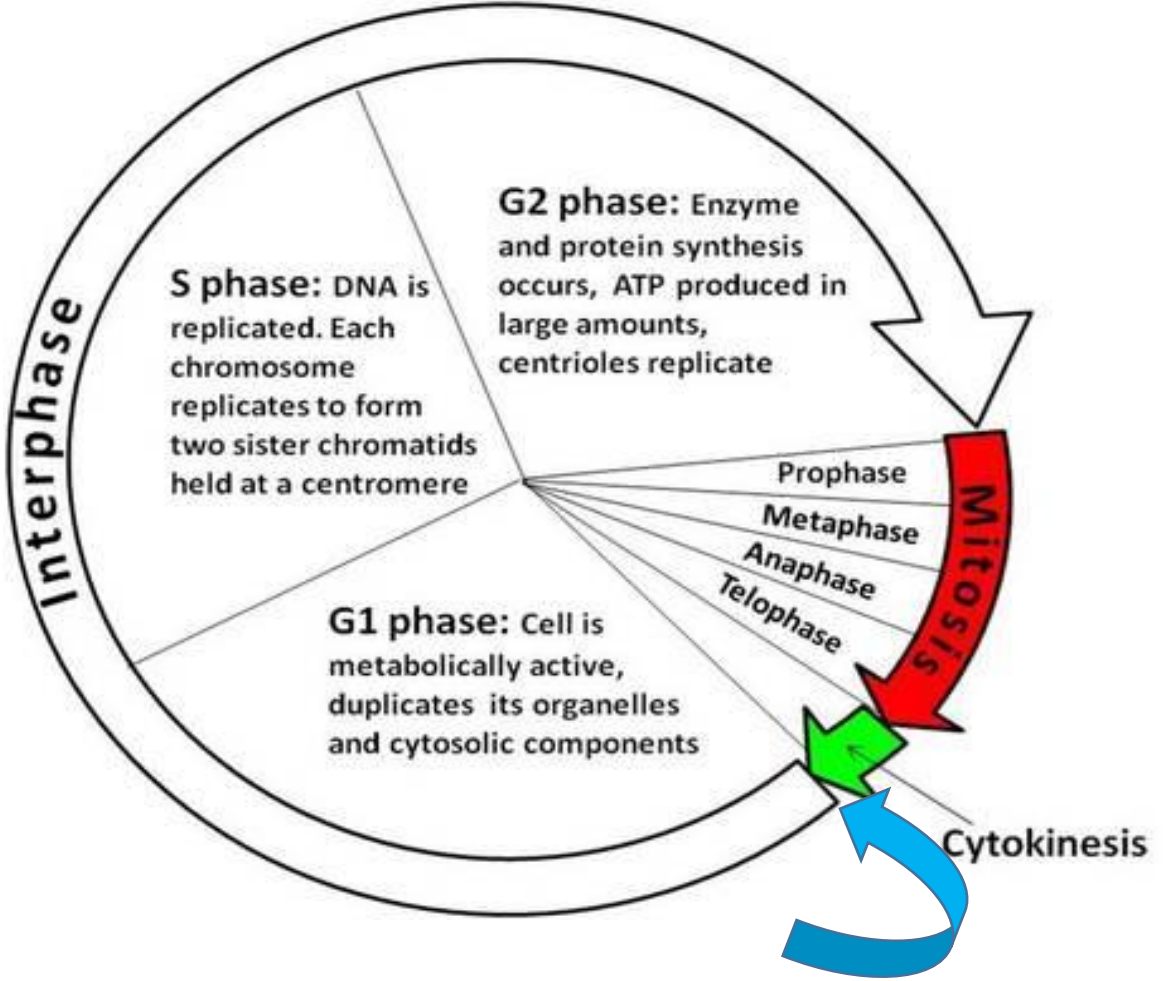
Cell cycle?

Orderly sequence of cellular and molecular events in which it duplicates its contents

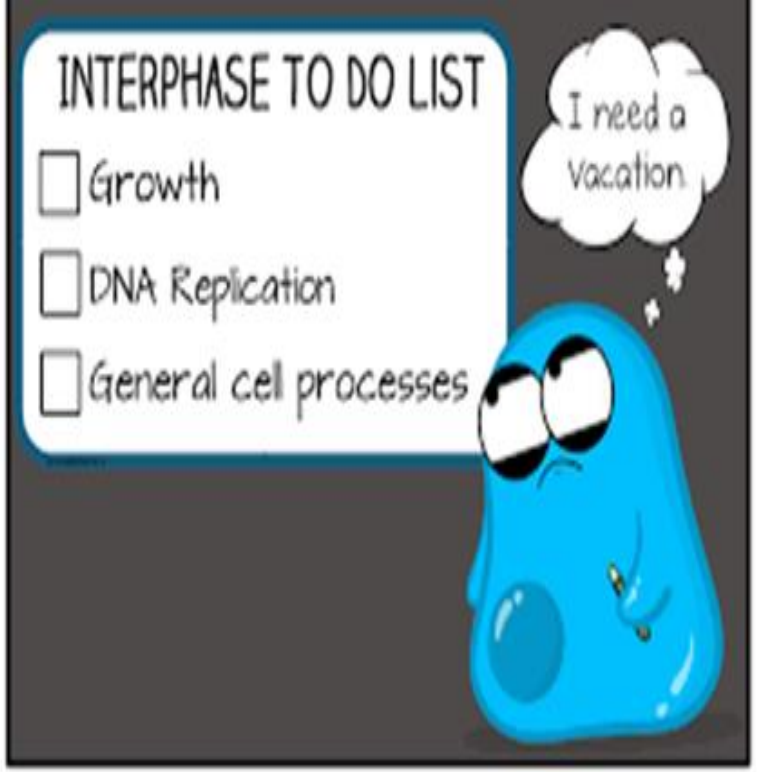


Cell cycle

- To divide, a cell must complete several important tasks: it must grow, copy its genetic material (DNA), and physically split into two daughter cells.
- TWO major phases:
  - **INTERPHASE:** cell grows and makes copy of its DNA.
  - **MITOTIC PHASE (M):** cell separates its DNA into two sets and divides its cytoplasm, forming two new cells.



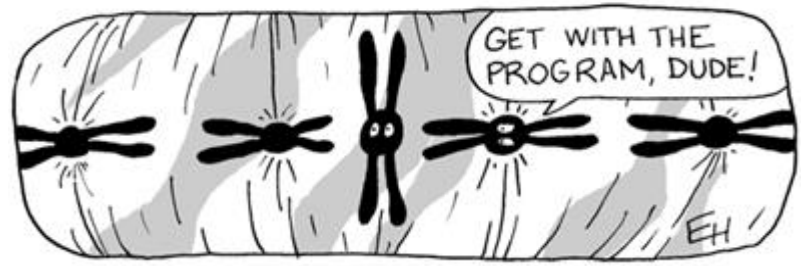
G_0 OR QUISCENT PHASE: Cell is not actively preparing to divide, it's just doing its job. G0 is a permanent state for some cells, while others may re-start division if they get the right signals.



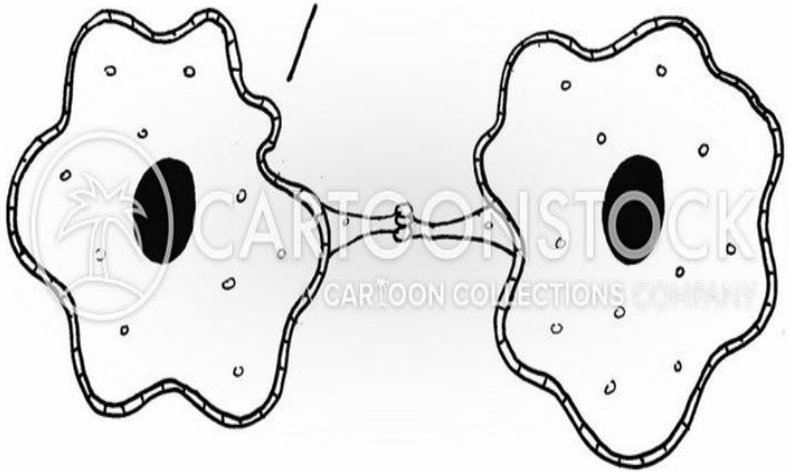
Prophase

Said the cell, "I'm not feeling quite right;"
My chromatins' wound really tight;
Both centrioles,
Are at opposite poles,
And my envelopes' fading from sight!

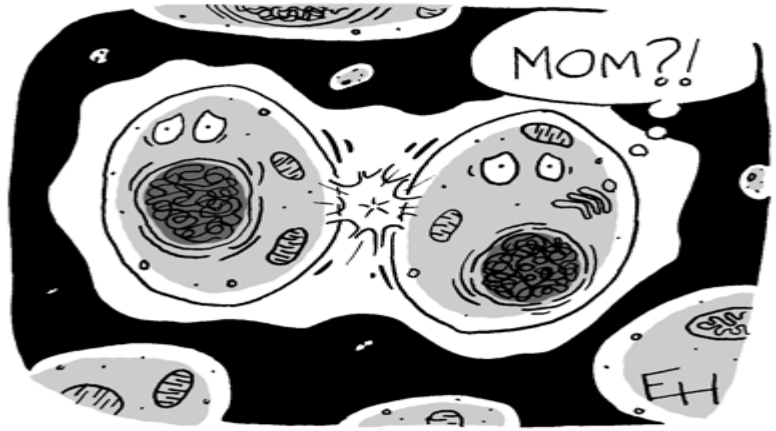
Metaphase



With kinetochores starting to grow,
The chromosomes all in a row,
Are tidy and straight,
On the metaphase plate,
With a spindle above and below.



Telophase

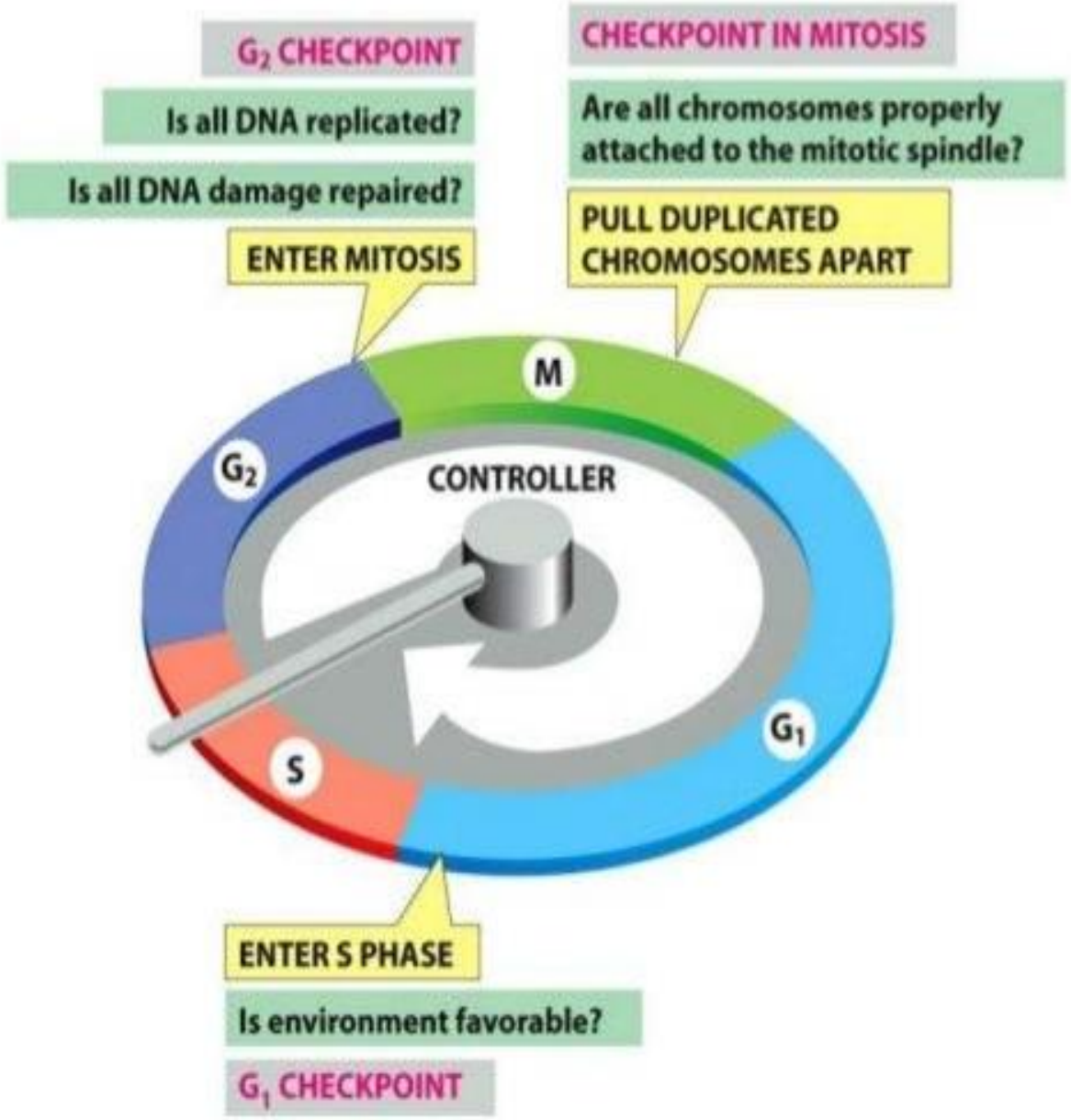


The daughter cells said, "We admit,
To being confused just a bit;
We've no father or brother,
And it seems that our mother,
Has quite unexpectedly split!"

Anaphase

A chomosome shaking with dread,
To her dear sister chromatid said,
"Though it's beaking my heart,
We'll be soon torn apart,
By a strong microtubule thread!"

Cell cycle check points



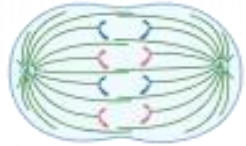
Different cell cycle checkpoints have evolved that prevent replication of damaged DNA and premature entry to or exit from mitosis, and allow time for DNA repair after encountering DNA damage.

The main cell cycle checkpoints are the

- **the G1/S checkpoint**
- **the G2/M checkpoint**
- **the spindle assembly checkpoint (SAC)**.

Cell Cycle Checkpoints

M Checkpoint



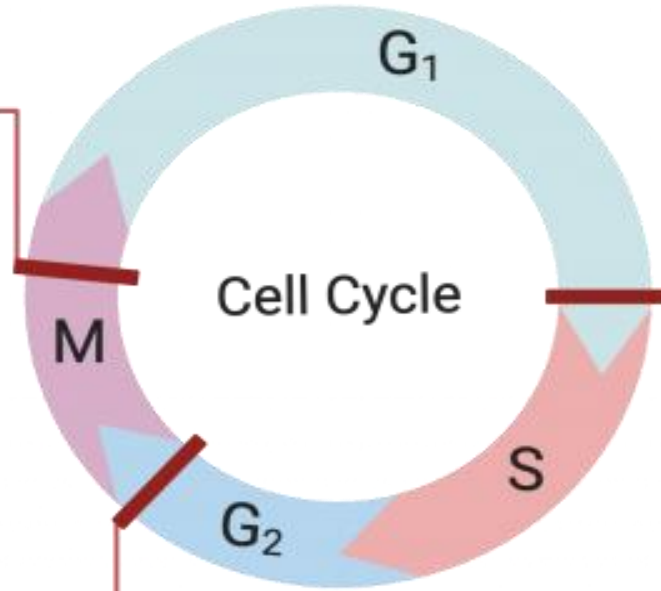
Pass
- Attachment of each kinetochore to a spindle fiber

Fail
- Chromatids are not properly assembled on mitotic spindle

G_1 Checkpoint

Pass
- Sufficient number of organelles
-Large cell volume

Fail
- DNA damage

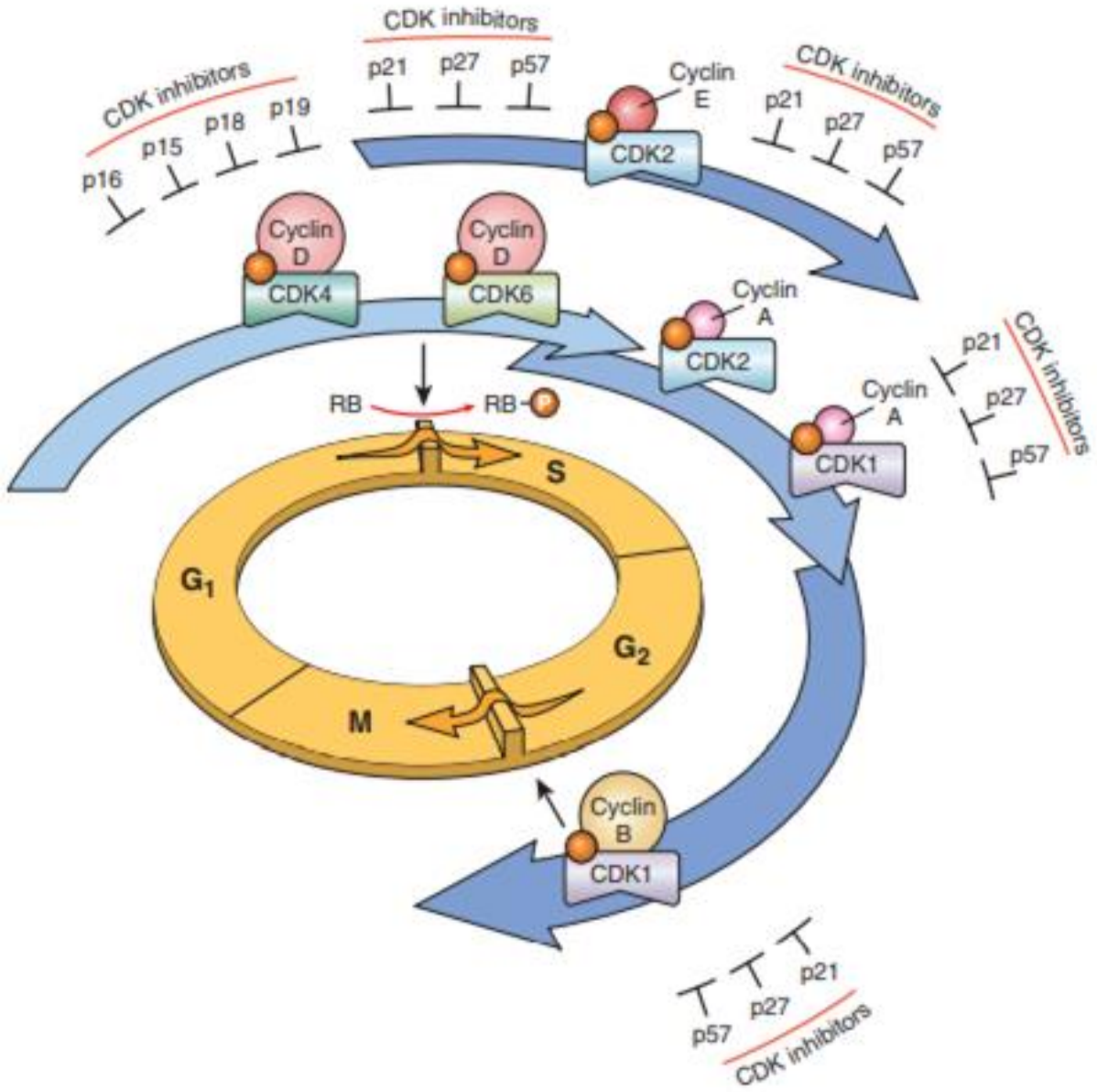


G_2 Checkpoint

Pass
- Completely replicated genome
- Large cell volume

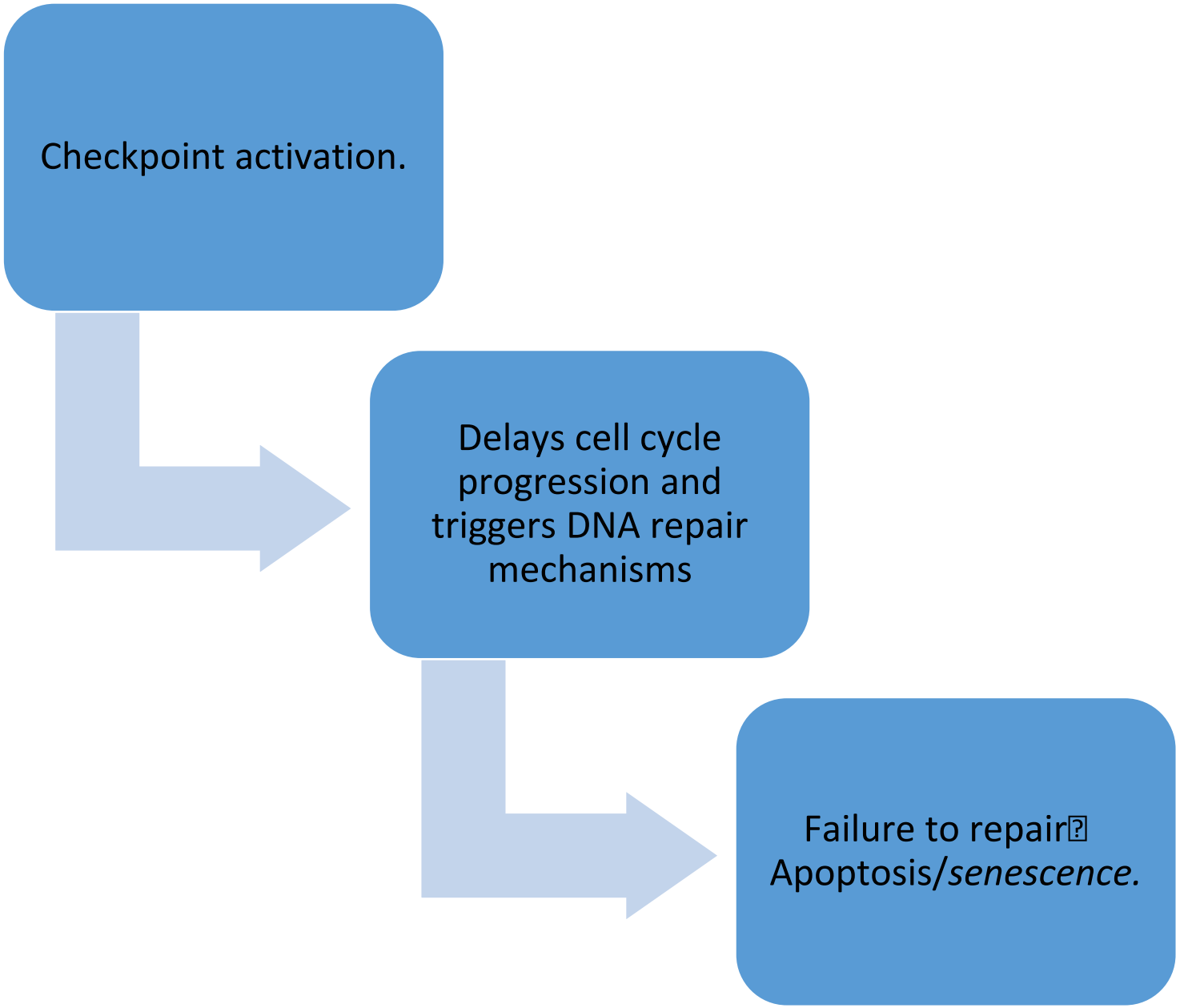
Fail
- DNA damage

Cell cycle control



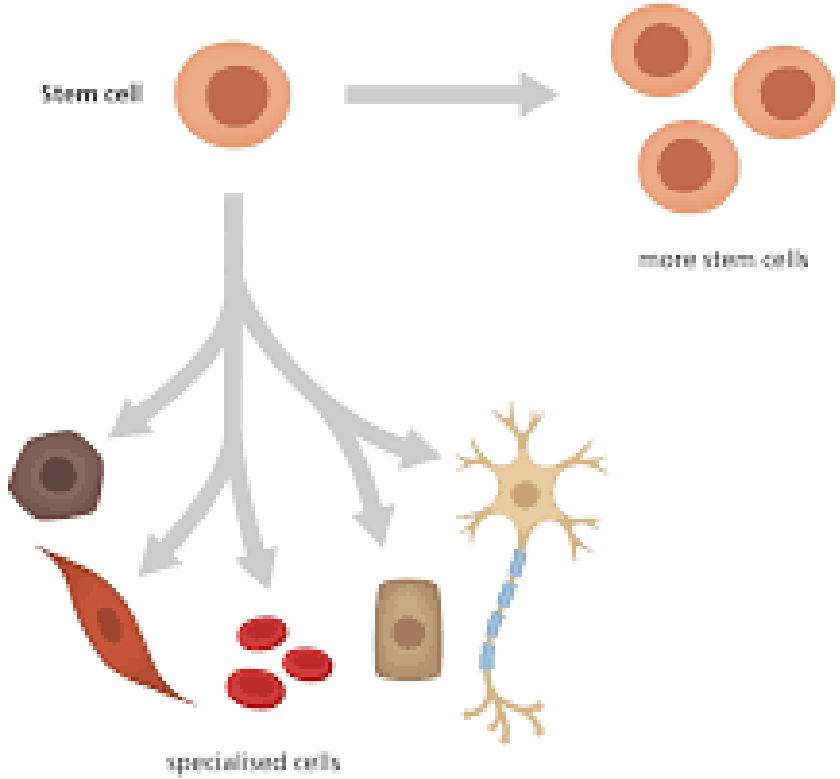
- Cell cycle progression is driven by proteins called cyclins— named for the cyclic nature of their production and degradation and cyclin-associated enzymes called cyclin dependent kinases (CDKs).
- The tumor suppressor pathways p53 and retinoblastoma (RB) control the DNA damage response.
- RB promotes cell cycle arrest in G1 and regulates entry into S phase
- p53 mediates several effects, including causing G1 and G2 arrest and promoting apoptosis.

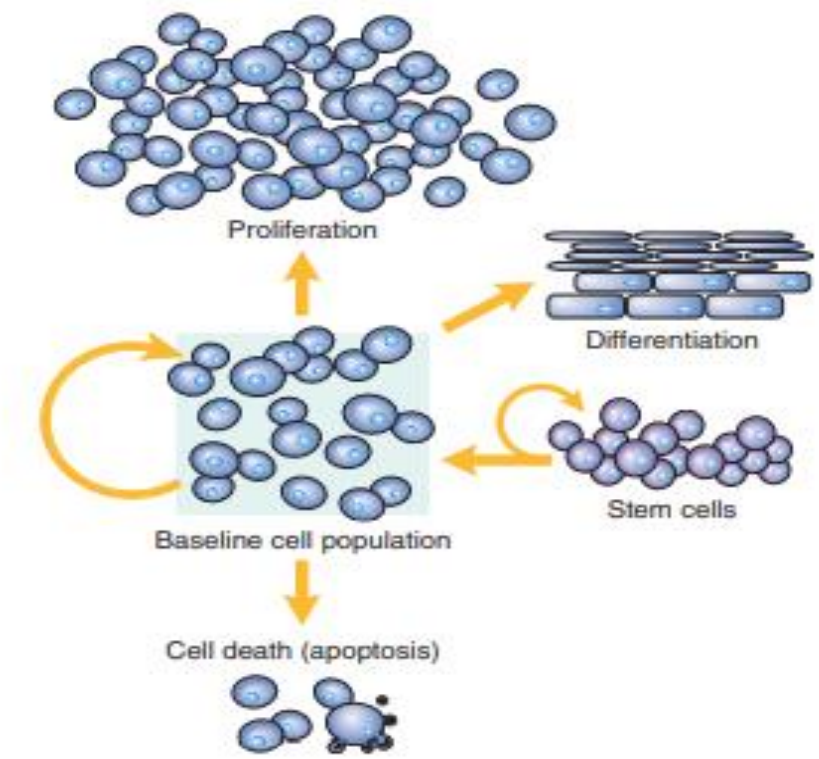
Cell Proliferation



Stem cells

Stem cell, an undifferentiated cell that can divide to produce some offspring cells that continue as stem cells and some cells that are destined to differentiate (become specialized). Stem cells are an ongoing source of the differentiated cells that make up the tissues and organs of animals and plants.





Stem cells are characterized by two important properties:

- Self-renewal, which permits stem cells to maintain their numbers.
- Asymmetric division, in which one daughter cell enters a differentiation pathway and gives rise to mature cells, while the other remains undifferentiated and retains its self-renewal capacity

REGENERATIVE MEDICINE

The ability to identify, isolate, expand, and transplant stem cells has given birth to the new field of regenerative medicine. Theoretically, the differentiated progeny of ES or adult stem cells can be used to repopulate damaged tissues, or to construct entire organs for replacement.

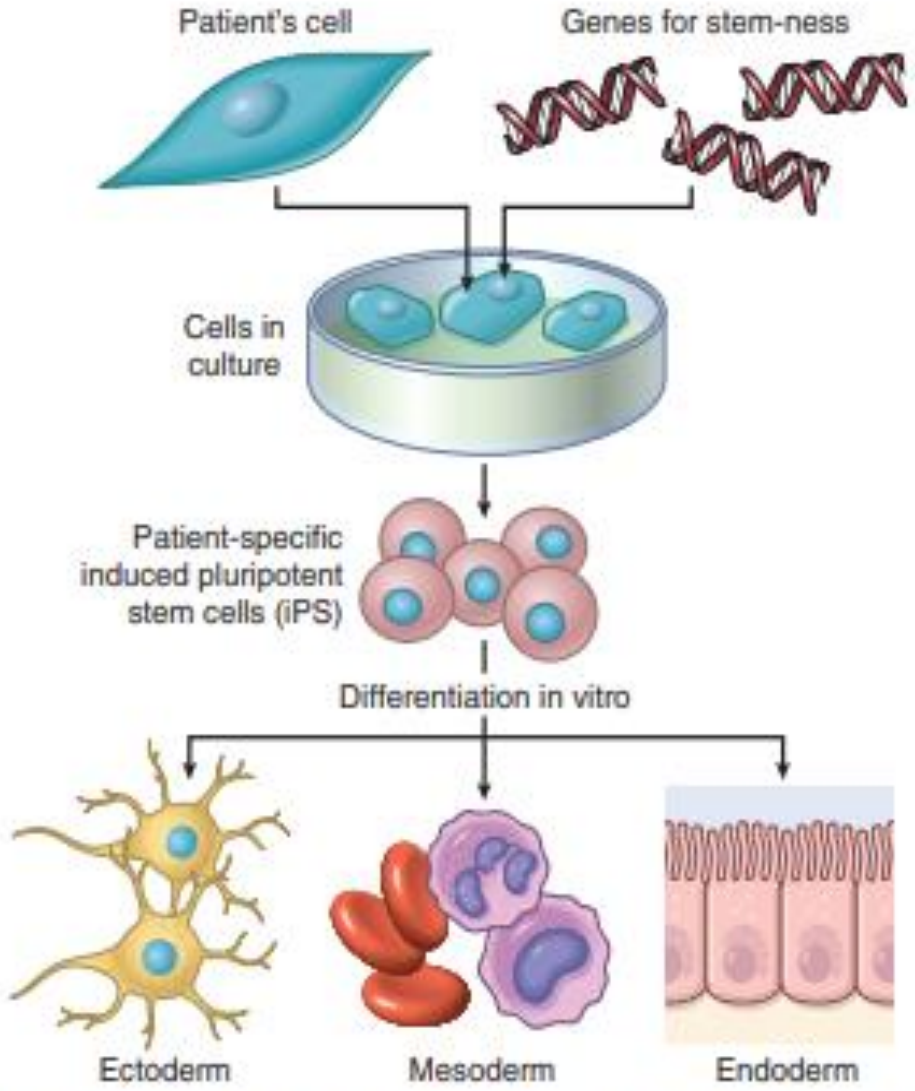


Figure 1-22 The production of induced pluripotent stem cells (iPS cells). Genes that confer stem cell properties are introduced into a patient's differentiated cells, giving rise to stem cells that can be induced to differentiate into various lineages. (Modified from Hochedlinger K, Jaenisch R: Nuclear transplantation, embryonic stem cells, and the potential for cell therapy. N Engl J Med 349:275-286, 2003.)

Case Study

A 35 years old male came to the OPD with complaints of Persistent, painless swelling in the cervical region for the past 3 months. There is no history of fever, weight loss, or night sweats. No history of chronic infections or recent travel.

On Clinical Examination there is a 3 cm firm, non-tender, mobile cervical lymph node with no hepatosplenomegaly and no signs of systemic illness

Further investigation reveals a fine-needle aspiration cytology (FNAC) of the lymph node, which shows an increased mitotic index, large atypical lymphoid cells, and loss of cell cycle control markers

DIAGNOSIS??????????????

LYMPHOM
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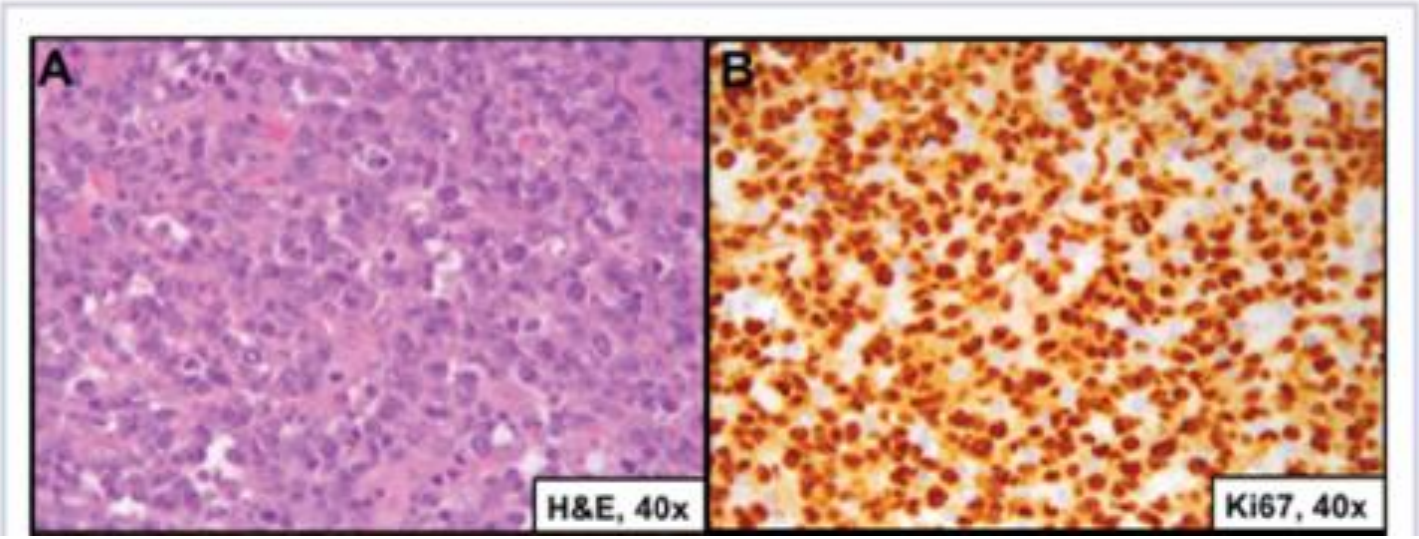

1- How does dysregulation of the cell cycle contribute to uncontrolled cell proliferation in neoplastic conditions?

A-The cell cycle is tightly regulated by cyclins, cyclin-dependent kinases (CDKs), and checkpoints (G1/S and G2/M).Dysregulation due to mutations in tumor suppressor genes (e.g., TP53, RB1) or overactivation of proto-oncogenes (e.g., MYC, RAS) removes cell cycle control.

2-What role do proto-oncogenes (e.g., MYC) and tumor suppressor genes (e.g., TP53) play in malignancies?

A- Proto-oncogenes (e.g., MYC, RAS, EGFR):Normally regulate cell growth and differentiation. Gain-of-function mutations convert them into oncogenes, leading to excessive proliferation and survival. Tumor suppressor genes (e.g., TP53, RB1, BRCA1/2):Function as cell cycle regulators and apoptosis inducers. Loss-of-function mutations remove growth inhibition, allowing uncontrolled cell proliferation.TP53 (guardian of the genome) is frequently mutated in cancers, leading to defective DNA repair and apoptosis.

3- How can Ki-67 and mitotic index be used to assess cell proliferation?

A- Ki-67: A nuclear protein expressed in actively dividing cells (G1, S, G2, and M phases, but absent in G0).High Ki-67 index correlates with aggressive tumors (e.g., high-grade lymphomas, breast cancer).

4- What are the pathological differences between reactive lymphadenopathy and lymphoma?

Feature	Reactive Lymphadenopathy	Lymphoma
Cause	Response to infection, autoimmune disease	Neoplastic proliferation of lymphoid cells
Architecture	Preserved normal nodal structure	Effaced lymph node architecture
Cellularity	Polyclonal lymphocytes, plasma cells	Monoclonal lymphoid proliferation
Mitotic Activity	Low to moderate	High (in aggressive types)
Immunophenotyping	Mixed B and T cells	Clonal B/T cell expansion

Additional Read