

Plasma Membrane

- Barrier for cell
- Facilitates and restricts **cellular exchange** of substances
- Maintains **electrochemical gradient** and receptors for signal transduction
- Lipid bilayer consisting of **phospholipids, cholesterol and proteins**

Nucleus

- Contains **genetic code**
- Controls cell division and functions**
- Composed of **DNA and proteins**

Three **components**:

The chromatin, the nuclear envelope, and the nucleoli

- Largest organelle**
- Site of DNA replication and transcription**
- Has an **affinity for basic dyes** (deep purple with wright stain)

Nucleolus

- Synthesizes ribosomal RNA** and assembles ribosome subunits
- Composed of **ribosomal RNA**

Ribosomes

- Synthesizes proteins**
- Composed of **protein and ribosomal RNA**

Rough Endoplasmic Reticulum

- Synthesizes most membrane-bound proteins**
- Studded with ribosomes**
- Membrane-lined tubules that **branch and connect to nuclear membrane**

Smooth Endoplasmic Reticulum

- Synthesizes phospholipids and steroids**
- Detoxifies drugs; stores calcium**
- No ribosomes**
- Membrane-lined tubules **adjacent/touching with RER**

Membrane Carbohydrates

In the outer layer, carbohydrates (oligosaccharides) are covalently linked to some membrane proteins:

Carbohydrates + protein = **glycoproteins**

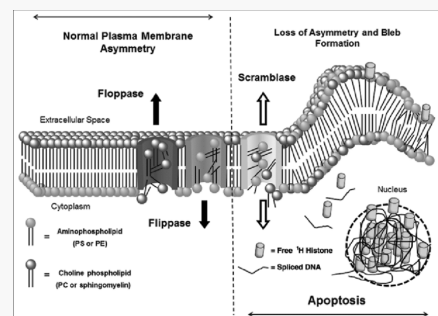
Carbohydrates + phospholipids = **glycolipids**

Glycoprotein + glycolipid = **glycocalyx**

Glycocalyx provide a **negative surface charge**

Glycoprotein and glycolipid are **surface markers or antigens**

Phospholipid Asymmetry in the Membrane



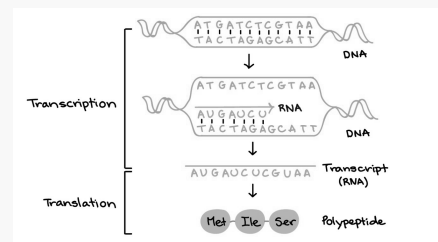
Phosphatidylserine + Phosphatidylethanolamine = inner layer

Sphingomyelin + Phosphatidylcholine = outer layer

Nucleus: Nuclear Envelope

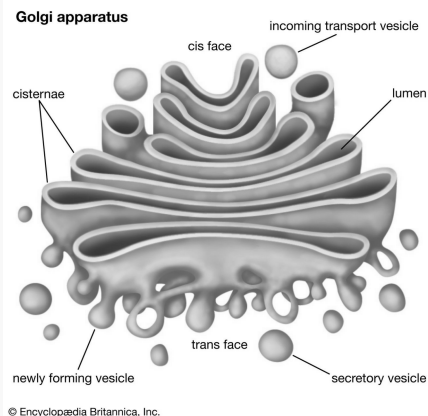
Have **nuclear pore** = passage of molecules between the nucleus and the cytoplasm

Nucleus: Nucleoli



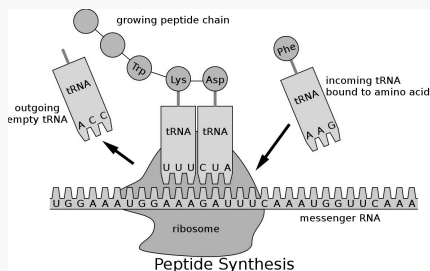
- Site of ribosomal RNA (rRNA) production
- Nucleolus produce ribosome>ribosome create protein># of nucleoli = protein synthesis that occurs
- Mature cells = decreased protein synthesis

Golgi Apparatus



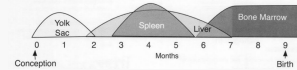
- Stack of flattened sacs called cisternae
- Modify, sort, and pack macromolecules for secretion or delivery to other organelles
- Vesicles that contains membrane-bound and soluble proteins from RER > enter golgi (cis face) > modified by enzymes either for glycosylation, sulfation, or phosphorylation > exit golgi (trans face) > lysosomes/secretory vesicles are formed > go to plasma membrane

Cytoplasm



- tRNA carry and transport amino acid to the ribosome
- mRNA provides the genetic code for the sequence of amino acids for the protein being synthesized
- Cells that produce proteins = increased ribosome = dark blue stain (basophilia)
- Therefore, RBC precursor produce hb (a protein)>more basophilic>darker

Hematopoiesis



Hematopoiesis

Bone marrow

3rd trimester to adulthood

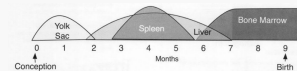
Stromal cells

- Protects BM
- Secrete many different growth factors required for stem cell, progenitor cell, and precursor cell survival
- Creates an extracellular matrix = By secreting collagen, fibronectin, thrombospondin, laminin, and proteoglycans (such as hyaluronate, chondroitin sulfate, and heparan sulfate)

Growth factors (ligands)

- Regulate the proliferation and differentiation of progenitor and precursor cells
- Bind to a receptor>signals nucleus>activate kinase>promote response (proliferate/differentiate)

Hematopoiesis



Tumor Suppressor Genes

Code proteins that ensure and control cell division only when required

Loss of function of tumor suppressor gene = uncontrolled cell division = cancer

TP53 - Most important Tumor suppressor gene

- Detects G1 DNA damage
- Trigger apoptosis
- Ensures only DNA-error free cells can undergo division
- TP53 > Inc TP21 > inhibits cyclin/cdk complex > no cell division occurs

Regulation of the Cell Cycle

Needed to prevent abnormal or mutated cells from going through the cell cycle and producing an abnormal clone

FOUR MAJOR CHECKPOINTS IN THE CELL CYCLE

- **G1 restriction point** - checks for the appropriate amount of nutrients and appropriate cell volume
- **G1 DNA damage checkpoint** - checks the DNA for damage and makes the cell wait for DNA repair or initiates apoptosis.
- **G2 DNA damage checkpoint** - verify that replication took place without error or damage (defects=mitosis is blocked)
- **Mitosis metaphase** - checks the alignment of chromosomes and the integrity of the spindle apparatus. (defects=anaphase is blocked)

Mitosis

Prophase

- Chromosomes condense
- Duplicated centrosomes begin to separate
- Mitotic spindle fibers appear

Prometaphase

- Nuclear envelope disassembles
- Centrosomes move to opposite poles
- Sister chromatids attach to the mitotic spindle fibers

Metaphase

- Sister chromatids align

Anaphase

- Sister chromatids separate and move on opposite poles

Telophase

- Mitotic spindle fibers disappear
- Nuclear membrane reassembles

Cytokinesis

- Cell divides into two identical daughter cells

Mitochondria

- Produces most of the cell's **ATP** via **oxidative phosphorylation**

Capable of self-replication

An organelle that has its own DNA and RNA

Cristae - oxidative enzymes are attached

Mitochondrial enzymes:

- oxidize pyruvate and fatty acids to acetyl CoA
- citric acid cycle oxidizes the acetyl CoA producing electrons for the electron transport pathway

Lysosomes

- Contains **hydrolytic enzymes** that degrade unwanted material in the cell

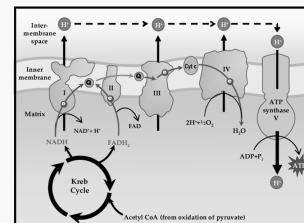
Lysosomal enzymes

- Low pH cytosol (acidic) = active
- High pH (bcontain hydrolytic enzymes (intracellular digestive process))

Lysosomal lipid storage diseases

- Gaucher disease
- Tay-Sachs disease

Mitochondria



Microfilaments

- Supports **cytoskeleton and motility**

- Double-stranded, intertwined solid **structures of actin**

Microfilaments and Intermediate Filaments

- Supports **cytoskeleton and motility**
- Double-stranded, intertwined solid **structures of actin**

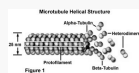
Actin microfilaments

- 5 to 7 nm in diameter
- associate with myosin to enable cell motility, contraction, and intracellular transport.
- near the nuclear envelope to assist in cell division
- near the plasma membrane to provide cytoskeletal support

Intermediate filaments

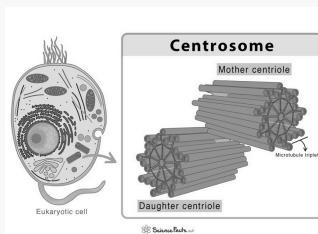
- 8 to 10 nm diameter
- most durable element of the cytoskeleton
- provide structural stability for the cells
- Found in keratins and lamins

Microtubules



- Maintains **cell shape, motility, and mitotic process**
- Form the mitotic spindle fibers during mitosis and are the major components of centrioles.
- Hollow cylinder of α and β tubulin forming 13 protofilaments

Centrosome



- Contains centrioles that serve as insertion points for mitotic spindle fibers
- Two cylinder-shaped centrioles at **right angle; nine bundles of three microtubules.**

Cell Membrane

Polar-charged hydrophilic (water-soluble) structures	Phospholipid's phosphate end + cholesterol's hydroxyl radical
Non-polar-charged hydrophobic (water-insoluble) structures	Phospholipid's fatty acid chains + cholesterol's steroid nucleus

Membrane Proteins

1. Transmembrane proteins

- Channels and transporters for water, ions, and other molecules between the cytoplasm and the external environment.
- Also function as receptors and adhesion molecules.
- Have cytoplasmic ends to attach the cytoskeletal proteins = structural integrity to the cell

2. Cytoskeletal proteins

- Found only on the cytoplasmic side of the membrane

Example: Hereditary spherocytosis

Inherited gene mutation that codes for transmembrane or cytoskeletal proteins > disrupt membrane integrity > short RBC life span > hemolytic anemia

Nucleus: Chromatin

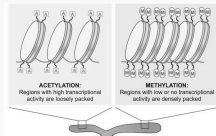
1. Heterochromatin

- Condensed clumping pattern
- Transcriptionally inactive
- Seen in mature cells = they are less transcriptionally active

2. Euchromatin

- Diffuse, uncondensed, open chromatin
- Genetically active
- Pale blue when stained with wright stain

Nucleus: Chromatin



CELL CYCLE

Purpose

- Replicate DNA
- Distribute identical chromosome copies equally to two daughter cells during mitosis

Biochemical and morphologic four-stage process

- G1 (gap 1), S (DNA synthesis), G2 (gap 2), and M (mitosis)

CELL CYCLE

G0 (quiescence)

- Cell is not actively in the cell cycle.
- Resting period until cell have right requirements to divide

G1

- Period of cell growth; synthesis of components necessary for replication
- Lasts about 10 hours

S stage

- DNA replication takes place
- 8 hours
- Produces sister chromatids
- Centrosome is also duplicated

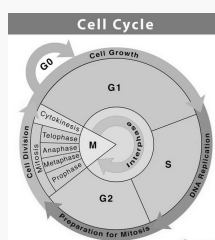
G2

- The tetraploid DNA is checked for proper replication and damage
- 4 hours

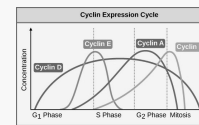
M stage

- Division of chromosomes and cytoplasm into two daughter cells.

CELL CYCLE



Cyclin/CDK complexes



1. Cyclin (protein) binds to CDK (enzymes)
2. Cyclin-CDK complex activate the proteins required in progression of cell cycle

Via phosphorylation (Phosphate group attach to target proteins)

- G1 – cyclin D + cdk4 and cdk6
- G1 going to S phase – cyclin E + cdk2
- S phase to G2 – cyclin e (decrease) Cyclin A (increase) + cdk2 and cdk1
- Mitosis – Cyclin B + cdk1

NECROSIS AND APOPTOSIS

Necrosis - direct external injury to cells

- Cell swell
- Nucleus lyse
- Membrane no integrity
- Pathologic – cell injury

Apoptosis - self-inflicted cell death from the cell itself

- Cell shrink
- Nucleus condenses
- Membrane intact
- Physiologic – remove unwanted/unneeded cell