

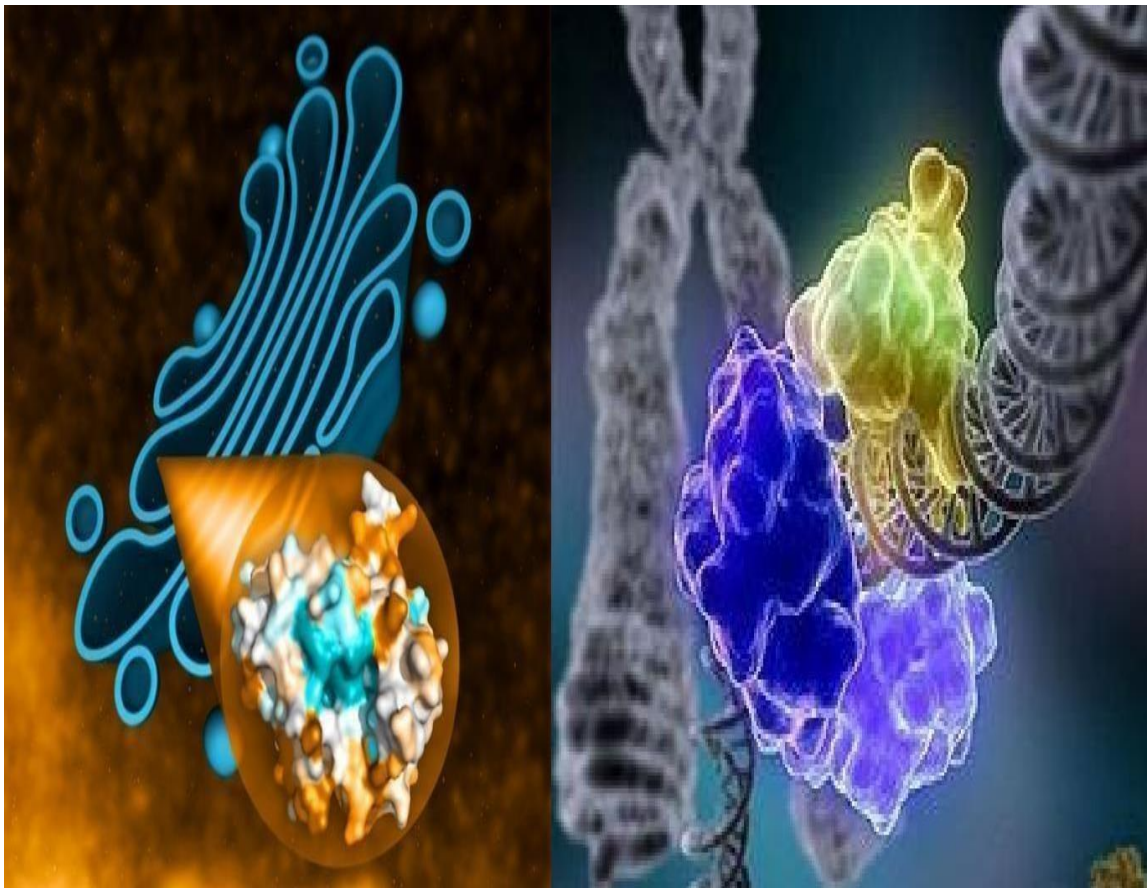
REPUBLIC ALGERIAN DEMOCRATIC AND POPULAR
Ministry of Higher Education and Scientific Research

University of Abbes Laghrour-Khenchela

Faculty of Natural and Life Sciences
Biology Molecular and Cellular Department



Tutorial Handouts for Cellular and Functional Biochemistry



Level: 3rd Year Licence Biochemistry

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List of abbreviations

- **ATP:** Adenosine Triphosphate
- **ADP:** Adenosine Diphosphate
- **cAMP:** cyclic Adenosine Monophosphate
- **cGMP:** cyclic Guanosine Monophosphate
- **DNA:** Deoxyribonucleic Acid
- **RNA:** Ribonucleic Acid
- **mRNA:** messenger RNA
- **rRNA:** ribosomal RNA
- **tRNA:** transfer RNA
- **hnRNA:** heterogeneous nuclear RNA
- **NADH:** Nicotinamide Adenine Dinucleotide (Reduced)
- **FADH₂:** Flavin Adenine Dinucleotide (Reduced)
- **ER:** Endoplasmic Reticulum
- **RER:** Rough Endoplasmic Reticulum
- **SER:** Smooth Endoplasmic Reticulum
- **GPI:** Glycosylphosphatidylinositol
- **ECM:** Extracellular Matrix
- **ETC:** Electron Transport Chain
- **V-ATPase:** Vacuolar-type Adenosine Triphosphatase
- **GPCR:** G Protein-Coupled Receptor
- **RTK:** Receptor Tyrosine Kinase
- **GAP:** GTPase-Activating Protein
- **GEF:** Guanine nucleotide Exchange Factor
- **PKA:** Protein Kinase A
- **PKC:** Protein Kinase C
- **PKG:** Protein Kinase G
- **PLC:** Phospholipase C
- **PLA₂:** Phospholipase A₂
- **PIP₂:** Phosphatidylinositol 4,5-bisphosphate
- **IP₃:** Inositol Trisphosphate
- **DAG:** Diacylglycerol
- **MAPK:** Mitogen-Activated Protein Kinase
- **MAPKK:** MAPK Kinase (e.g., MEK)
- **MAPKKK:** MAPKK Kinase (e.g., Raf)
- **ERK:** Extracellular signal-Regulated Kinase
- **SH₂:** Src Homology 2 domain
- **SH₃:** Src Homology 3 domain
- **PTB:** Phosphotyrosine-Binding domain
- **Grb₂:** Growth factor receptor-bound protein 2
- **SOS:** Son of Sevenless
- **IRS:** Insulin Receptor Substrate
- **COX:** Cyclooxygenase

- **NO:** Nitric Oxide
- **PARs:** Protease-Activated Receptors
- **Hsp90:** Heat Shock Protein 90
- **NLS:** Nuclear Localization Signal
- **EGFR:** Epidermal Growth Factor Receptor
- **EGFRvIII:** Epidermal Growth Factor Receptor variant III
- **PI3K:** Phosphoinositide 3-Kinase

Preface

Designed for the third-year Cellular and Functional Biochemistry tutorials, this handout offers a comprehensive journey from foundational principles to the forefront of biochemical research. Key themes include cellular organization, membrane dynamics, signal transduction, and the chemical basis of genetics. To connect theory with real-life application, the material includes different learning tools like problem-solving exercises, critical thinking questions, and multiple-choice questions (MCQs) with answers keys, all designed to help students gain a deep, practical understanding of the syllabus.

Chapter 1: Functional Compartmentalization of the Cell

This chapter establishes the fundamental principles of eukaryotic cell biology, emphasizing the correlation between structure and function.

- **Cell Theory:** Reinforces that the cell is the basic unit of life, where all biochemical activities are highly coordinated within and by its internal structures. It highlights that all living organisms are composed of cells, and that cells arise from pre-existing cells.
- **Cellular Diversity:** Distinguishes between prokaryotic cells (structurally simple, lacking a membrane-bound nucleus and organelles) and eukaryotic cells (complex, with a defined nucleus and numerous membrane-bound organelles). A comparative analysis highlights key differences in size, DNA structure (circular vs. linear, associated with histones), ribosome size (70S vs. 80S), and internal compartmentalization.
- **Endosymbiotic Theory:** Explains the evolutionary origin of key eukaryotic organelles, specifically mitochondria and chloroplasts, which are believed to have originated from symbiotic prokaryotes (alpha-proteobacteria and cyanobacteria, respectively) engulfed by a primitive host cell. Evidence includes their own circular DNA, double membranes, and 70S ribosomes.
- **Cellular Components:** Describes the structure and specialized functions of major organelles:
 - **Nucleus:** Surrounded by a double membrane (nuclear envelope) perforated by nuclear pores, it houses the cell's genetic material (DNA) organized into chromosomes and is the site of DNA replication and transcription.
 - **Cytoplasm & Cytosol:** The cytoplasm is the entire content within the cell membrane, excluding the nucleus. The cytosol is the viscous liquid phase of the cytoplasm, where many metabolic reactions occur.
 - **Endoplasmic Reticulum (ER):** An extensive network of membranes. The Rough ER (RER) is studded with ribosomes and is the primary site for the synthesis and initial processing of secretory and membrane proteins. The Smooth ER (SER) is involved in lipid synthesis, steroid hormone production, and detoxification of drugs and poisons.
 - **Golgi Apparatus:** A stack of flattened membranous sacs (cisternae) that functions as a processing and sorting center. It modifies proteins and lipids from the ER (e.g., by glycosylation), packages them into vesicles, and directs them to their final destinations (lysosomes, plasma membrane, or secretion).

- **Mitochondria:** The "powerhouses of the cell," surrounded by a double membrane. The inner membrane is highly folded into cristae to increase surface area. Mitochondria are the site of aerobic cellular respiration, comprising the citric acid cycle (in the matrix) and oxidative phosphorylation (on the inner membrane), which generates the majority of cellular ATP.
- **Lysosomes & Peroxisomes:** **Lysosomes** are acidic organelles containing a suite of hydrolytic enzymes (acid hydrolases) for the breakdown of macromolecules, aged organelles (autophagy), and ingested particles (phagocytosis). **Peroxisomes** contain oxidative enzymes (e.g., catalase) that break down fatty acids and neutralize toxic compounds like hydrogen peroxide.
- **Cytoskeleton:** A dynamic network of protein filaments that provides structural support, determines cell shape, facilitates intracellular transport, and enables cell motility. It comprises microfilaments (actin), intermediate filaments (various proteins providing mechanical strength), and microtubules (tubulin, involved in vesicle transport and forming the mitotic spindle).

Chapter 2: Biomembranes

This chapter delves into the molecular composition, dynamic structure, and fundamental properties of biological membranes.

- **Composition:** Membranes are complex assemblies of lipids (~40-50%), proteins (~50-60%), and carbohydrates (~5-10%, attached to lipids or proteins). The main lipid classes are phospholipids (forming the bilayer backbone), glycolipids, and cholesterol(modulates fluidity).
- **Membrane Proteins:** Classified based on their interaction with the lipid bilayer:
 - **Integral/Transmembrane Proteins:** Span the entire bilayer, often as alpha-helices or beta-barrels. They function as channels, transporters, and receptors.
 - **Peripheral Proteins:** Temporarily associated with the membrane surface, typically bound to integral proteins or lipid head groups via ionic or other non-covalent interactions. They are often involved in signaling or as components of the cytoskeleton.
 - **Lipid-anchored Proteins:** Covalently attached to lipid molecules (e.g., glycosylphosphatidylinositol, GPI anchors) that are embedded in the bilayer.
- **Fluid Mosaic Model:** Describes the membrane as a two-dimensional fluid in which lipids and proteins can diffuse laterally. The model also emphasizes asymmetry, meaning the lipid and protein composition differs between the inner and outer leaflets. Fluidity is regulated by temperature, cholesterol content (increases fluidity at low temperatures and decreases it at high temperatures), and the degree of fattyacid saturation (unsaturated fattyacids increase fluidity).
- **Membrane Carbohydrates:** Found exclusively on the extracellular face, attached to proteins (glycoproteins) or lipids (glycolipids), forming the glycocalyx. This carbohydrate coat is crucial for cell-cell recognition, adhesion, and protection against mechanical and chemical damage.

Chapter 3: Cell Structure-Function Relationship

This chapter integrates specific cellular structures with their precise biochemical roles, illustrating how cellular architecture enables complex functions.

- **Protein Synthesis & Secretion:** Details the secretory pathway: mRNA is translated by ribosomes bound to the RER; the nascent polypeptide is translocated into the ER lumen for folding, glycosylation, and quality control; correctly folded proteins are transported via vesicles to the Golgi apparatus for further modification and sorting; finally, they are packaged into secretory vesicles and released from the cell via exocytosis.
- **Cytoskeleton:** Elaborates on the roles of the three filament systems. Microfilaments (Actin) are involved in cell motility, cytokinesis, and forming microvilli. Intermediate Filaments provide mechanical strength and anchor organelles. Microtubules form tracks for motor proteins (kinesin, dynein) that transport vesicles and organelles, and are essential for forming the mitotic spindle. Focal adhesions are large macromolecular assemblies that link the intracellular actin cytoskeleton to the extracellular matrix (ECM) via transmembrane integrins, transducing mechanical and chemical signals.
- **Muscle Contraction:** Explains the sliding filament theory at the molecular level. Upon neural stimulation, calcium release triggers the interaction between actin (thin filaments) and myosin (thick filaments) in the sarcomere. Myosin heads, powered by ATP hydrolysis, undergo a conformational change ("power stroke") that pulls the actin filaments inward, leading to sarcomere shortening and muscle contraction.
- **Mitochondria & Oxidative Phosphorylation:** Provides a detailed look at the process of ATP synthesis. The electron transport chain (ETC), consisting of four complexes (I-IV) in the inner mitochondrial membrane, uses energy from electrons (derived from NADH and FADH₂) to pump protons into the intermembrane space, creating an electrochemical gradient. ATP synthase (Complex V) uses the energy of protons flowing back into the matrix (chemiosmosis) to phosphorylate ADP, producing ATP.
- **Ribosomes & Protein Addressing:** Ribosomes, composed of rRNA and proteins, are the molecular machines for protein synthesis. The signal hypothesis explains how proteins destined for secretion or organelles are targeted. The Golgi apparatus acts as a central sorting hub, using specific molecular tags like mannose-6-phosphate to direct enzymes to lysosomes, or other signals to target proteins to the plasma membrane or secretory vesicles.
- **Lysosomal System:** Lysosomes are not just degradative compartments but are integral to cellular homeostasis. Their acidic pH (maintained by V-ATPase pumps) optimizes hydrolase

activity. They are involved in autophagy (recycling cellular components), heterophagy (degrading phagocytosed material), antigen presentation in immunity, and repair of the plasma membrane.

Chapter 4: Glycosylation of Macromolecules and Biological Role

This chapter covers the enzymatic process of glycosylation and its critical biological implications.

- **Glycoproteins:** Proteins covalently modified with oligosaccharide chains. Glycosylation occurs primarily in the ER and Golgi apparatus.
 - **N-linked Glycosylation:** The carbohydrate is attached to the amide nitrogen of an asparagine residue in the sequence Asn-X-Ser/Thr. It begins in the ER with a core oligosaccharide.
 - **O-linked Glycosylation:** The carbohydrate is attached to the hydroxyl oxygen of serine or threonine residues. It is primarily initiated and elaborated in the Golgi apparatus.
- **Biological Roles of Glycosylation:**
 - **Protein Folding & Stability:** Assists in proper protein folding in the ER and protects against proteolysis.
 - **Cell-Cell Recognition & Adhesion:** Carbohydrate moieties on cell surfaces act as specific ligands for receptors like selectins and other lectins.
 - **Glycocalyx Formation:** Creates a protective and lubricating cell coat.
 - **Intracellular Trafficking:** Serves as a specific "zip code" for targeting proteins to correct organelles, e.g., the mannose-6-phosphate tag for lysosomal targeting.
- **Examples:**
 - **Blood Group Antigens:** The A, B, and O antigens are glycan structures present on glycolipids and glycoproteins on red blood cells. The specificity is determined by the terminal sugar (N-acetylgalactosamine for A, galactose for B, absence of both for O).
 - **Lectins:** Carbohydrate-binding proteins that are not enzymes or antibodies. They are classified into types like C-type (Calcium-dependent, e.g., selectins), P-type (bind mannose-6-phosphate), and I-type (immunoglobulin superfamily lectins, e.g., sialoadhesin), and are pivotal in cell adhesion, signaling, and pathogen recognition.

Glycolipids: Membrane lipids with covalently bound carbohydrate chains. They are classified as neutral glycolipids (e.g., cerebroside, with a single sugar) and acidic glycolipids (e.g., gangliosides, which contain one or more sialic acid residues and are particularly abundant in the nervous system, playing roles in cell recognition and signal transduction).

Chapter 5: Signal Transduction and Regulation of Cell Function

This comprehensive chapter explores the molecular mechanisms by which cells perceive, transmit, and respond to extracellular signals.

- **Signaling Types:** Classified by the distance over which the signal acts:
 - **Endocrine:** Hormones travel long distances via the bloodstream (e.g., insulin).
 - **Paracrine:** Local mediators act on nearby cells (e.g., neurotransmitters, histamine).
 - **Autocrine:** Cells respond to signals they themselves secrete (common in cancer and immune cells).
 - **Synaptic:** A specialized paracrine signaling where neurotransmitters are released across a synaptic cleft.
- **Receptors and Ligands**
 - **Ligands:** Signaling molecules (e.g., hormones, growth factors, cytokines). Hydrophilic ligands bind to cell-surface receptors; hydrophobic ligands (e.g., steroid hormones, thyroid hormones) can cross the membrane and bind to intracellular receptors.
 - **Receptors**
 - **Nuclear Receptors:** Function as ligand-activated transcription factors for steroid and thyroid hormones.
 - **Ion Channel-Receptors:** Ligand-gated channels that open upon binding, allowing ion flux (e.g., nicotinic acetylcholine receptor).
 - **G Protein-Coupled Receptors (GPCRs):** A large family of 7-transmembrane receptors that activate intracellular heterotrimeric G proteins.
 - **Enzyme-Linked Receptors:** Typically, single-transmembrane receptors with intrinsic or associated enzymatic activity (e.g., Receptor Tyrosine Kinases (RTKs) which dimerize and autophosphorylate upon ligand binding).
- **Signal Transduction Components**
 - **Transducers: G proteins** act as molecular switches. Heterotrimeric G proteins ($G\alpha$, $G\beta$, $G\gamma$) associate with GPCRs. Small monomeric G proteins (e.g., Ras) are activated by other receptors like RTKs. Their GTP-bound state is active, and hydrolysis to GDP returns them to an inactive state, a cycle regulated by GAPs (GTPase-Activating Proteins) and GEFs (Guanine nucleotide Exchange Factors).
 - **Adapter and Scaffolding Proteins:** Proteins like Grb2, SHC, and IRS contain modular domains (SH2 domains bind phosphotyrosine, SH3 domains bind proline-rich motifs, PTB

domains also bind phosphotyrosine) that physically link activated receptors to downstream effectors, ensuring specificity and efficiency in the signaling cascade.

- **Second Messengers & Amplification Cascades**

- **cAMP Pathway:** Ligand → GPCR → Gs protein → Activation of Adenylate Cyclase → generation of cAMP → activation of Protein Kinase A (PKA) → phosphorylation of target proteins.
- **Phospholipase C (PLC) Pathway:** Ligand → GPCR → Gq protein → Activation of PLC-β → hydrolysis of PIP₂ into IP₃ (diffuses to ER, releasing Ca²⁺) and DAG (remains in membrane, activating Protein Kinase C, PKC).
- **Eicosanoid Pathway:** Activation of Phospholipase A2 (PLA2) releases arachidonic acid from membrane phospholipids. Arachidonic acid is then converted by cyclooxygenases (COX) to prostaglandins or by lipoxygenases to leukotrienes, potent local mediators of inflammation and other processes.
- **cGMP Pathway:** Involves gaseous messengers like Nitric Oxide (NO), which diffuses into cells and activates soluble guanylate cyclase, producing cGMP, which then activates Protein Kinase G (PKG) and other effectors, leading to vasodilation.
- **MAP Kinase Pathway:** A critical pathway for cell proliferation and differentiation, often initiated by RTKs: Ligand → RTK dimerization/autophosphorylation → Recruitment of adapter proteins (Grb2/SOS) → Activation of Ras → Activation of Raf (MAPKKK) → Phosphorylation of MEK (MAPKK) → Phosphorylation of ERK (MAPK) → Translocation to the nucleus → Phosphorylation of transcription factors → Altered gene expression.

Chapter 6: Signaling Abnormality and Pathology

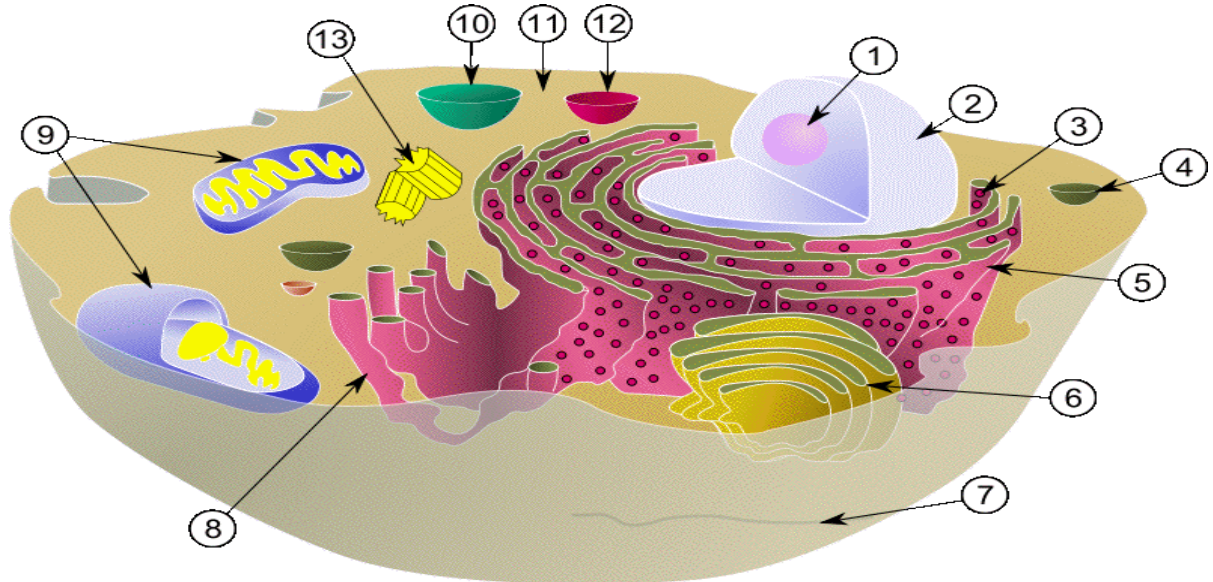
This chapter connects molecular defects in signaling pathways to the pathogenesis of human diseases, with a focus on cancer.

- **Oncogenes:** These are gain-of-function mutations in normal cellular genes called proto-oncogenes. The mutated versions (oncogenes) drive uncontrolled cell growth and survival. Examples include hyperactive forms of Ras (point mutations) and EGFR (overexpression or mutations).
- **EGFR in Cancer:** The Epidermal Growth Factor Receptor is a proto-oncogene frequently dysregulated in cancers. Abnormal activation can occur via gene amplification, overexpression, or constitutive activating mutations (e.g., EGFRvIII deletion mutant). This leads to ligand-independent, continuous activation of downstream pro-growth and pro-survival pathways like RAS/MAPK and PI3K/AKT, promoting tumorigenesis in lung, colorectal, and breast cancers.
- **RAS/MAPK Pathway Pathology:** Mutations in the KRAS gene are among the most common oncogenic drivers in human cancers (e.g., >90% of pancreatic cancers, ~40% of colorectal cancers). These mutations, often at glycine 12, impair the GTPase activity of Ras, locking it in a perpetually active GTP-bound state. This results in continuous signaling through the MAPK pathway, driving proliferation independent of upstream growth factor signals. Crucially, these mutations confer resistance to therapies targeting upstream receptors, such as anti-EGFR monoclonal antibodies (e.g., Cetuximab).

Tutorial N° 1

Exercise 1

a) Label the figure opposite (numbers 1 to 13).



b) What else would a plant cell contain?

c) A eukaryotic cell is a cell:

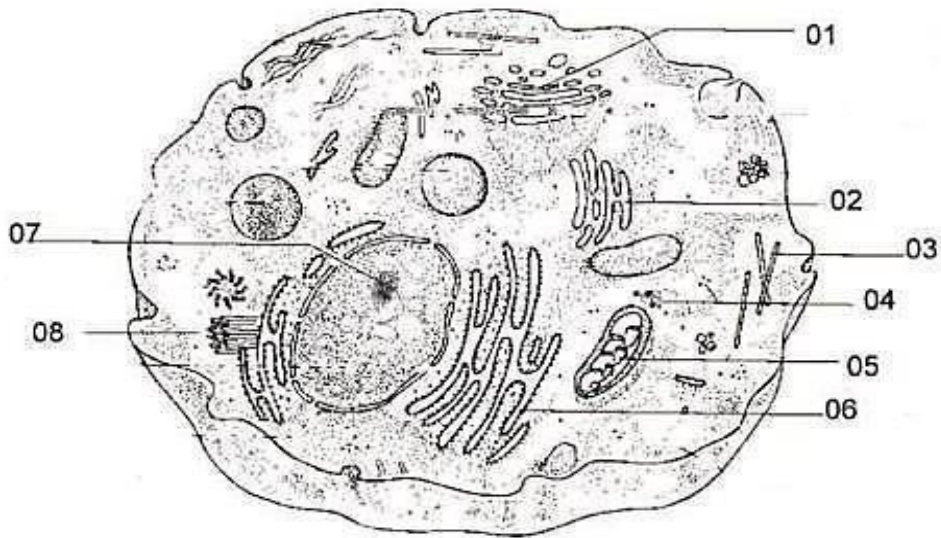
- 1) having a nucleoid;
- 2) compartmentalized;
- 3) comprising a cytoskeleton and achieving endomembrane flow.

Exercise 2

1) In the form of a comparative table, indicate the main characteristics of a prokaryotic cell and a eukaryotic cell, highlighting their major differences. Then, complete these tables with the appropriate answers.

Features	prokaryotic cell	eukaryotic cell
Typical size	μm	μm
Core type		
Cell division		
Genetic organization		
Nuclear membrane		
Number of chromosomes		
Circular chromosome		
Histones		
Nucleolus		
RNA and protein synthesis		
First amino acid initiating the synthesis of a polypeptide chain		
Cellular structures and organelles		
Endoplasmic reticulum		
Golgi apparatus		
Lysosomes		
Mitochondria		
Chloroplasts		
Microtubules		
Localization of ribosomes		
Functional attributes		
Phagocytosis		
Pinocytosis		
Cell movement		

2) Using the number codes from the drawing, complete the table below:



Indicate:	Code
A) where the assembly of ribosome subunits takes place;	
B) where glycosylation of proteins and lipids takes place;	
C) the structures where the synthesis of proteins encoded by nuclear DNA takes place (or even begins);	
D) the structure that allows vesicular traffic in the cell;	
E) the organelle responsible for the total oxidation of carbohydrates or fatty acids;	
F) the site of lipid synthesis;	
G) the organelle absent in plant cells.	

Tutorial N° 1 – Correction**Exercise 1**

a) Label the figure opposite (numbers 1 to 13).

Based on a standard eukaryotic cell diagram, the labels are likely as follows:

1. Nuclear Pore
2. Chromatin / DNA
3. Nucleolus
4. Nucleus
5. Rough Endoplasmic Reticulum (RER)
6. Golgi Apparatus
7. Secretory Vesicle
8. Plasma Membrane
9. Ribosomes (on the RER)
10. Cytosol / Cytoplasm
11. Lysosome
12. Mitochondrion
13. Smooth Endoplasmic Reticulum (SER)

b) What else would a plant cell contain?

A plant cell would also contain **chloroplasts**, a large central **vacuole**, and a **cell wall** made of cellulose.

c) A eukaryotic cell is a cell:

- 2) compartmentalized;
- 3) comprising a cytoskeleton and achieving endomembrane flow.

Exercise 2

- 1) Comparative table of prokaryotic and eukaryotic cells

Features	Prokaryotic Cell	Eukaryotic Cell
Typical size	1-10 μm	10-100 μm
Core type	Nucleoid	True Nucleus
Cell division	Binary Fission	Mitosis / Meiosis
Genetic organization	Single circular chromosome	Multiple linear chromosomes

Nuclear membrane	Absent	Present
Number of chromosomes	One (single chromosome)	More than one
Circular chromosome	Yes	No (linear)
Histones	No (DNA-associated with different proteins)	Yes
Nucleolus	Absent	Present
RNA and protein synthesis	Coupled (in the cytoplasm)	Separated (Transcription in nucleus, translation in cytoplasm)
First amino acid initiating polypeptide chain synthesis	Formyl-methionine	Methionine
Cellular structures and organelles		
> Endoplasmic reticulum	Absent	Present
> Golgi apparatus	Absent	Present
> Lysosomes	Absent	Present (in animal cells)
> Mitochondria	Absent	Present
> Chloroplasts	Absent	Present (in plant/algal cells)
> Microtubules	Absent	Present (part of the cytoskeleton)
Localization of ribosomes	Free in the cytoplasm (70S)	Free in cytosol or attached to RER (80S)
Functional attributes		
> Phagocytosis	Absent	Present (in some specialized cells)
> Pinocytosis	Absent	Present
> Cell movement	Flagella (simple, rotating)	Flagella/Cilia (complex, bending)

2) Using the number codes from the drawing:

Indicate:	Code
A) where the assembly of ribosome subunits takes place;	1
B) where glycosylation of proteins and lipids takes place;	5
C) the structures where the synthesis of proteins encoded by nuclear DNA takes place (or even begins);	3
D) the structure that allows vesicular traffic in the cell;	6
E) the organelle responsible for the total oxidation of carbohydrates or fatty acids;	7
F) the site of lipid synthesis;	4
G) the organelle absent in plant cells.	8

Tutorial N° 2

Exercise 1: Complete the following propositions:

A- In biological membranes, lipid molecules are arranged in a continuous double layer, called

B- The three major types of lipids found in cell membranes are

C- All lipids found in cell membranes are called because they have one end and one end

D....., lipids containing oligosaccharides, are found only on the outer face of the double layer, with their sugar groups exposed on the cell surface.

E- Proteins that extend across the double layer and are exposed to aqueous environments on either side of the membrane are called

F- The carbohydrate-rich zone on the surface of most eukaryotic cells is called

Exercise 2: Indicate whether the following assertions are true or false. If a proposition is false, explain why.

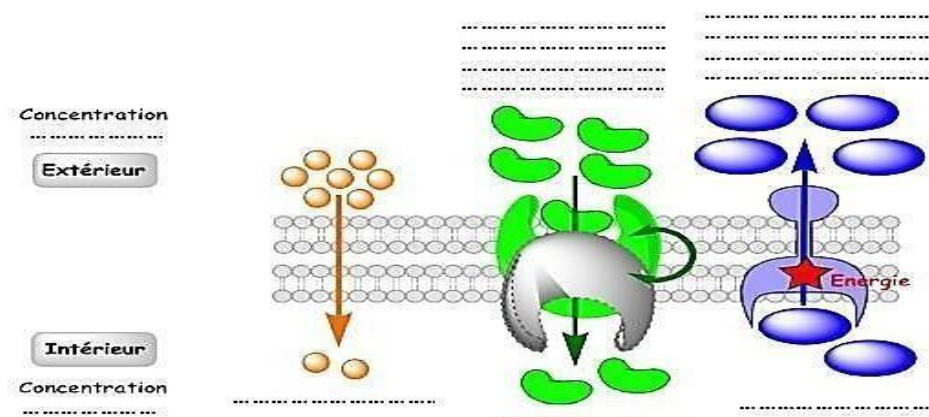
A- Maintaining the lipid double layer in the plasma membrane requires special enzymes and ATP hydrolysis.

B- The basic structure of biological membranes is determined by the lipid double layer, but their biological functions are linked to the presence of proteins.

C- In all cell membranes, the two lipid layers of the same bilayer have the same chemical composition, which is organelle-specific.

D- “Intrinsic” membrane proteins are proteins deeply and firmly embedded in the lipid bilayer.

Exercise 3: Fill in the gaps in the figures above:



Exercise 4: Answer this series of questions by placing a cross in front of the correct answer(s).

1- The plasma membrane is :

- a) A boundary between inside and outside
- b) A union between cells
- c) Exchange between cytosol and interstitial fluid

2- Which of the following molecules are not normal components of eukaryotic cell membranes?

- a) Proteins
- b) Glycogen
- c) Phospholipids
- d) Cholesterol
- e) Transfer RNA

3- The plasma membrane has :

- a) Two identical faces (identical molecular composition)
- b) Cholesterol molecules
- c) More carbohydrates than proteins
- d) DNA
- e) Phospholipids; partly polar, partly apolar structures

4- Among the following properties, tick the ones you think correspond to those of the plasma membrane (proteins and lipids):

- a) Barrier to most physiological solutes
- b) Attachment to extracellular matrix
- c) Lipid biosynthesis
- d) Non-fluid
- e) Receptivity to external environment

5- Membrane proteins:

- a) Are always transmembrane
- b) Can be transmembrane several times over
- c) Can be attached to the membrane by a lipid anchor (intrinsic membrane protein)
- d) Are highly glycosylated on the intracellular side
- e) Ensure selective transport across the membrane

6- Membrane proteins :

- a) are sometimes transmembrane
- b) are sometimes bound to the membrane, on the cytoplasmic side, by covalent bonding to a fatty acid or isoprenoid
- c) are all glycosylated
- d) are necessarily very hydrophobic
- e) are located only in the plasma membrane (not in organelles).

7- In eukaryotes, the plasma membrane comprises :

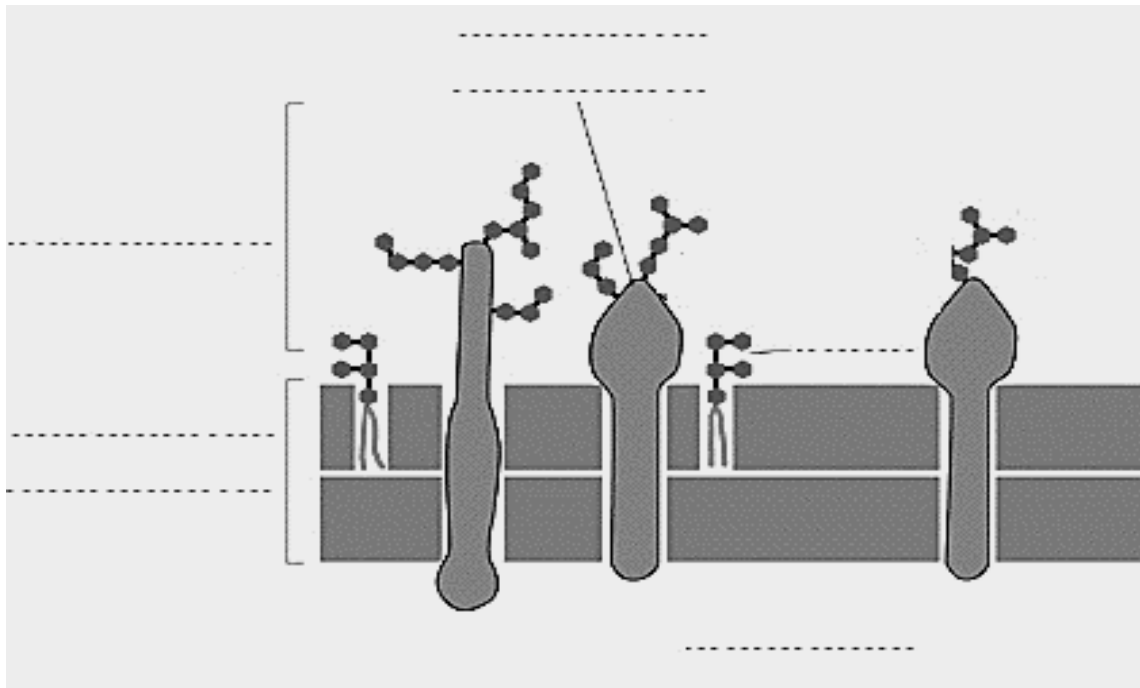
- a) Two lipid sheets of symmetrical molecular composition.
- b) Transporters and ion channels.
- c) Proteins that are uniquely transmembrane.

- d) A set of oligosaccharides on the cytoplasmic side.
- e) Cholesterol molecules influencing membrane fluidity.

8- Check off which of the following organelles are bounded by double membranes :

- a) Endoplasmic reticulum
- b) Nucleus
- c) Golgi apparatus
- d) Mitochondria
- e) Lysosome

Exercise 4: Fill in the gap in the figure above:



Tutorial N° 2 – Correction

Exercise 1: Complete the following propositions:

A- In biological membranes, lipid molecules are arranged in a continuous double layer, called **the lipid bilayer**.

B- The three major types of lipids found in cell membranes are **phospholipids, cholesterol, and glycolipids**.

C- All lipids found in cell membranes are called **amphipathic** because they have one **hydrophilic** end and one end **hydrophobic**.

D- Glycolipids, lipids containing oligosaccharides, are found only on the outer face of the double layer, with their sugar groups exposed on the cell surface.

E- Proteins that extend across the double layer and are exposed to aqueous environments on either side of the membrane are called **transmembrane proteins**.

F- The carbohydrate-rich zone on the surface of most eukaryotic cells is called **the glycocalyx**.

Exercise 2: Indicate whether the following assertions are true or false. If a proposition is false, explain why.

A- Maintaining the lipid double layer in the plasma membrane requires special enzymes and ATP hydrolysis.

False. The lipid bilayer forms and maintains its structure spontaneously in an aqueous environment due to the hydrophobic effect; it does not require energy input.

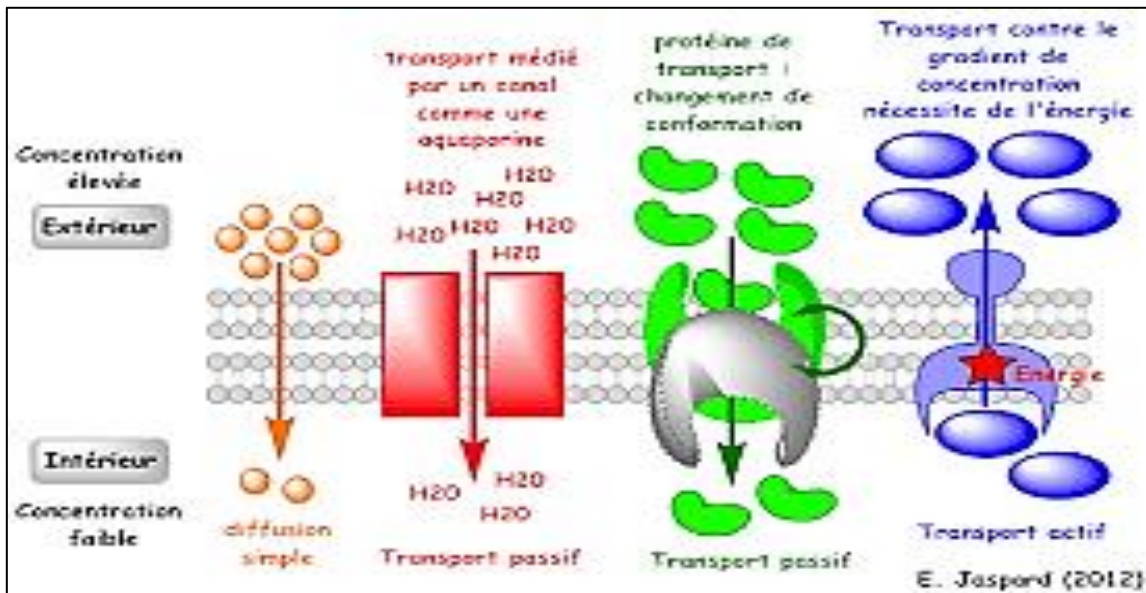
B- The basic structure of biological membranes is determined by the lipid double layer, but their biological functions are linked to the presence of proteins.
True.

C- In all cell membranes, the two lipid layers of the same bilayer have the same chemical composition, which is organelle-specific.

False. The two leaflets (monolayers) of the bilayer are asymmetrical, meaning they have different lipid compositions. This asymmetry is functional and maintained by the cell.

D- "Intrinsic" membrane proteins are proteins deeply and firmly embedded in the lipid bilayer.
True.

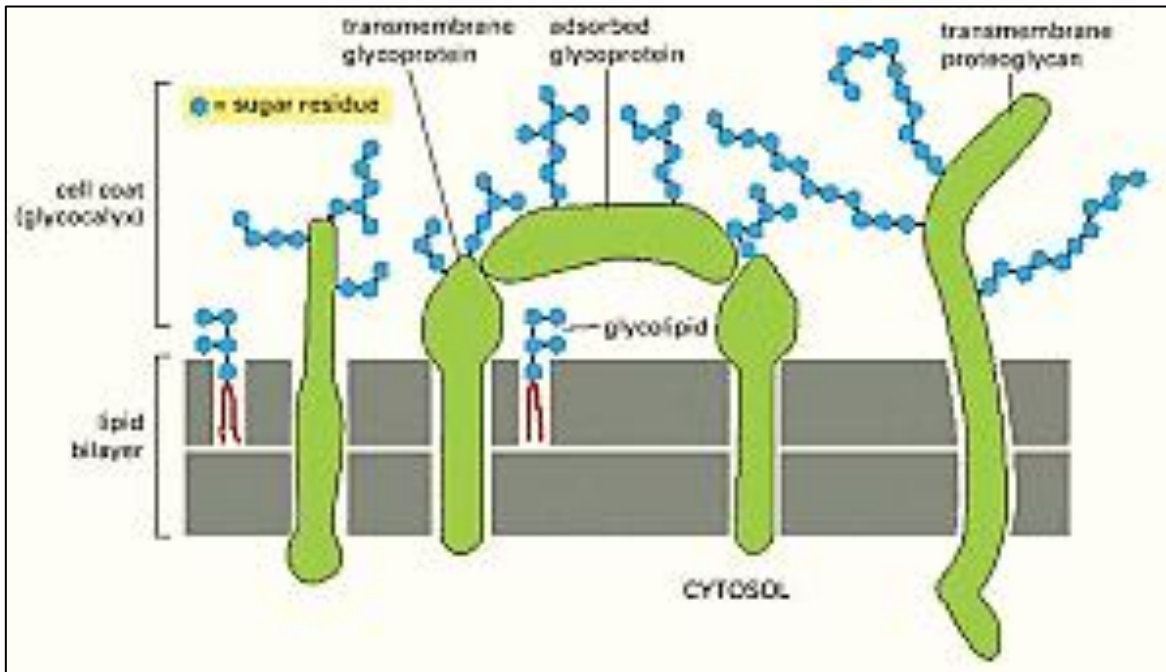
Exercise 3: Fill in the gaps in the figures above:



Exercise 4: Here are the correct answers for each question:

1.
 - a) A boundary between inside and outside
 - c) Exchange between cytosol and interstitial fluid
2.
 - b) Glycogen
 - e) Transfer RNA
3.
 - b) Cholesterol molecules
 - e) Phospholipids; partly polar, partly apolar structures
4.
 - a) Barrier to most physiological solutes
 - b) Attachment to extracellular matrix
 - e) Receptivity to external environment
5.
 - b) Can be transmembrane several times over
 - c) Can be attached to the membrane by a lipid anchor (intrinsic membrane protein)
 - e) Ensure selective transport across the membrane
6.
 - a) are sometimes transmembrane
 - b) are sometimes bound to the membrane, on the cytoplasmic side, by covalent bonding to a fatty acid or isoprenoid
7.
 - b) Transporters and ion channels
 - e) Cholesterol molecules influencing membrane fluidity
8.
 - b) Nucleus
 - d) Mitochondria

Exercise 4: Fill in the gap in the figure above:



Tutorial N° 3

Exercise 1: Select the appropriate one

1. Integrins are adhesion molecules

- a) They are expressed on the cell surface in the form of α and β dimers.
- b) Some of which bind to fibronectin (extracellular matrix).
- c) Are at the root of lateral adherens.
- d) Not expressed on endothelial cells.
- e) Are constantly active on leukocytes.

2. Adhesion molecules linked to their ligand (the counter-receptor)

- a) Signal to the cell interior
- b) prevent translocation of MAPkinases to the nucleus
- c) are expressed on the outer membrane of mitochondria
- d) play an important role in tissue integrity
- e) Induce apoptosis

3. Adhesion molecules play a role in

- a) cell survival
- b) cell and tissue integrity
- c) plasma membrane permeability
- d) circulation of leukocytes (white blood cells)
- e) organ formation during development

4. The extracellular matrix

- a) exists around all eukaryotic cells
- b) Is of cellular origin
- c) Always forms a loosely textured cellular environment in which cells can move
- d) Has a uniform composition in all tissues of the same individual
- e) Is basically made up of a combination of fibrous protein molecules and highly hydrated carbohydrate molecules.

5. The extracellular matrix is composed of

- a) glycosaminoglycans
- b) proteoglycans
- c) nucleic acids
- d) fibrous proteins
- e) membrane lipids

6. Among the constituents of the extracellular matrix

- a) Proteoglycans are associations of glycosaminoglycans covalently linked to a core protein.
- b) Glycosaminoglycans are made up of repetitively associated dimers.
- c) All fibrous proteins are proteoglycans.
- d) Collagen is a fibrous molecule rich in the amino acid hydroxyproline.
- e) Laminin enables specific cell attachments.

7. Among the roles of the extracellular matrix, we can mention the following

- a) resistance to crushing (compression resistance)

- b) Cell attachment support
- c) Support for cell migration
- d) Survival signal via adhesion molecules
- e) As a filter for molecules in the cellular environment

8. Collagen

- a) Represents a family of matrix proteins.
- b) Is the major constituent of the extracellular matrix.
- c) Provides resistance to tensile forces.
- d) Is consolidated by covalent bonds when fibrillar.
- e) Has elastic properties.

9. Cytoskeletal elements

- a) Are protein polymers.
- b) All have the same diameter
- c) Ensure the cell's overall shape.
- d) Form a static skeleton in the cell cytoplasm
- e) In the case of microtubules, can be involved in the intracellular movement of organelles.

10. Actin

- a) Is a dimeric protein made up of G-actin and F-actin
- b) Can polymerize into cylinders
- c) Polymerizes only in its ATP-binding form
- d) Also present in the cell nucleus in contact with the nuclear membrane, which it stabilizes
- e) Polymerizes into filaments exhibiting dynamic instability at their ends in vivo

11. Concerning muscle fibers

- a) striated muscle comprises numerous bundles of muscle fibers
- b) muscle fibers are anucleated
- c) each muscle fiber has contractile elements called myofibrils
- d) a myofibril is composed of several adjacent sarcomeres
- e) sarcomere contraction does not require nerve control

12. Striated muscle contraction

- a) Requires the presence of actin and myosin
- b) Can take place in the absence of calcium
- c) Involves shortening of sarcomeres
- d) Involves shortening of myosin filaments
- e) Results in actin filaments sliding over myosin filaments

13. Concerning sarcomeres

- a) The sarcomere is the contractile unit of striated and smooth muscle fibers.
- b) A sarcomere is delimited by two Z striae
- c) Fine filaments are made of myosin
- d) Myosin heads possess ATPase activity
- e) sarcomere contraction requires the presence of Ca^{2+} .

14. About mitochondria :

- a) On average, a mitochondrion is between 10 and 100 μm long.

- b) The mitochondrion is capable of synthesizing all its own proteins.
- c) The Krebs cycle produces NADH, ATP and CO₂
- d) Electron transfer enables H⁺ accumulation in the mitochondrial matrix
- e) In aerobic conditions, oxidative phosphorylation is not the cell's main source of ATP

15. Mitochondria

- a) ATP synthetase uses the sodium gradient.
- b) ATP synthetase is a biomolecular motor.
- c) Mitochondria contain DNA and ribosomes.
- d) Oxidative phosphorylation is the process by which electrons from NADH are transferred to ATP.
- e) Myopathies can be associated with mitochondrial dysfunction.

16. The mitochondrion

- a) Contains in its matrix the equipment necessary for protein synthesis
- b) Contains circular DNA
- c) Contains in its matrix the enzymatic equipment required for fatty acid biosynthesis
- d) Receives its phospholipids from the smooth ER via a phospholipid shuttle transporter
- e) Is the site of biosynthesis of certain steroid hormones

17. The mitochondrial inner membrane is characterized by

- a) Numerous ridges.
- b) The presence of highly permeable porins.
- c) High concentration of ATP synthetase.
- d) High concentration of cardiolipin and phosphatidylcholine.
- e) Integrins that bind with the cytoskeleton.

18. A nucleotide sequence is translated when it is in the form of

- a) DNA
- b) rRNA
- c) tRNA
- d) mRNA
- e) Heterogeneous nuclear RNA (hnRNA)

19. Ribosomal RNA (rRNA)

- a) are translated into ribosomal proteins
- b) are used for translation
- c) associate with ribosomal proteins to form ribosomes
- d) are partially transcribed in the nucleolus
- e) transport amino acids for protein synthesis

20. The amino acid sequence of a protein

- a) Is determined by the nucleotide sequence of its messenger RNA
- b) Is determined by the nucleotide sequence of its coding gene
- c) Strongly influences its shape (folding) and function
- d) Constitutes the primary structure
- e) Assembles in N-terminal direction C-terminal

21. Translation

- a) occurs in the nucleus

- b) requires messenger RNA (mRNA) and ribosomes
- c) requires the availability of amino acids (provided by transfer RNA)
- d) is produced from genomic DNA
- e) is specific to eukaryotes

22. Protein synthesis

- a) Requires the presence of the rough endoplasmic reticulum
- b) Can take place in the absence of mRNA
- c) Assembles amino acids in the N-terminal -> C-terminal direction
- d) Gives rise to a non-reducible polypeptide chain
- e) Requires the presence of transfer RNA

23. Golgi apparatus

- a) Maturates mRNAs.
- b) Carries out protein synthesis.
- c) Involved in post-translational protein maturation.
- d) Has numerous enzymes acting sequentially in deglycosylation and (re)glycosylation steps.
- e) Is an essential step in the formation and maturation of cytosolic and nuclear proteins.

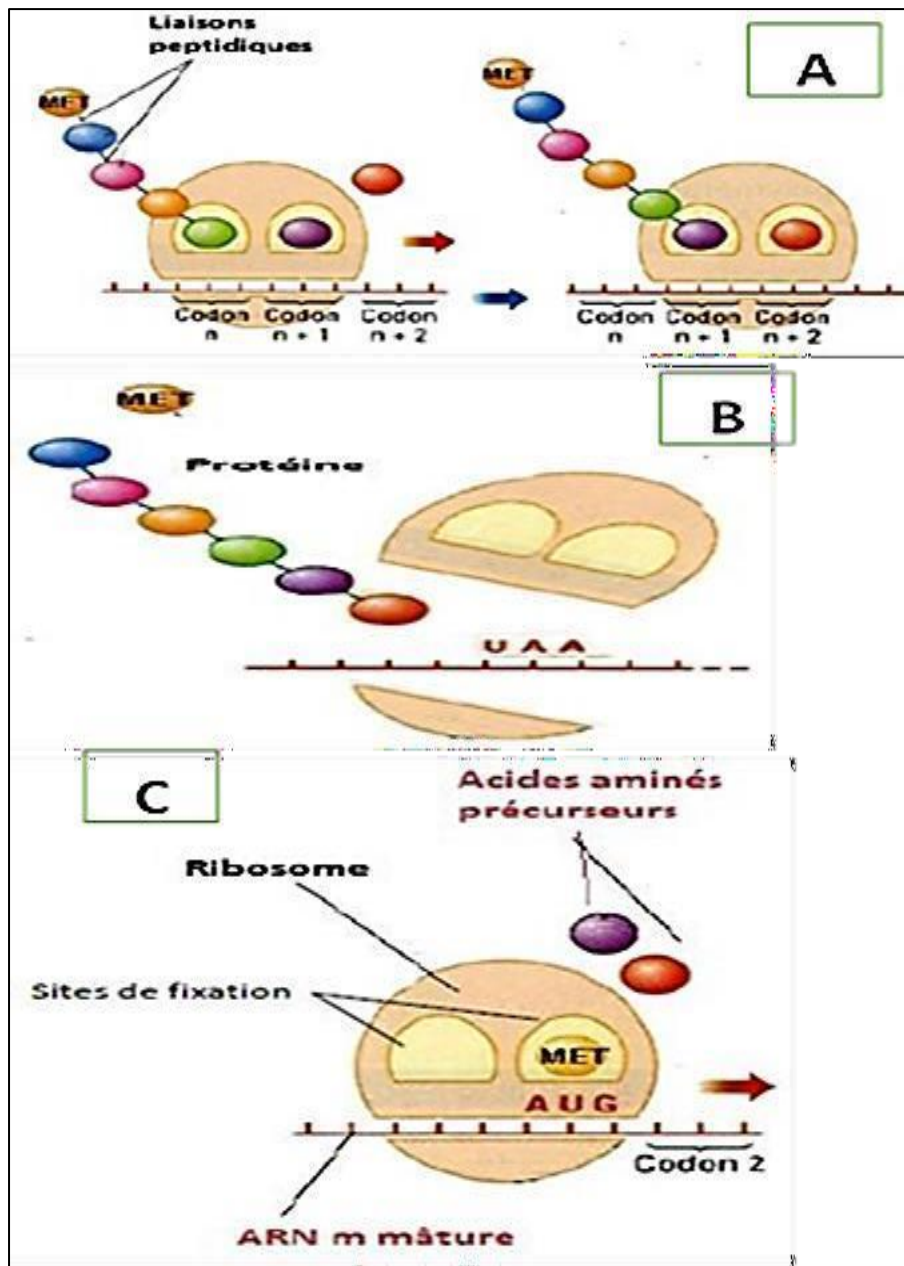
24. Lysosomes

- a) Are bounded by a double membrane
- b) Have a pH close to that of the cytosol
- c) Are formed by budding from the endoplasmic reticulum
- d) Contain hydrolytic enzymes (hydrolases)
- e) Digest only cytosolic products

25. Lysosomes

- a) Are permanently clathrin-coated vesicles
- b) Are ribosome-binding vesicles
- c) Use microtubular networks to move around the cell
- d) are the destination of mannose-6 phosphate-tagged proteins from the Golgi apparatus
- e) Contain a proton pump (ATPase H⁺ type V)

Exercice 2: Label and order the following diagrams:



Tutorial N° 3- Correction

Exercise 1: Here are the correct answers for each question:

1. Integrins are adhesion molecules
 - a) They are expressed on the cell surface in the form of α and β dimers.
 - b) Some of which bind to fibronectin (extracellular matrix).
2. Adhesion molecules linked to their ligand (the counter-receptor)
 - a) Signal to the cell interior
 - d) play an important role in tissue integrity
3. Adhesion molecules play a role in
 - a) cell survival
 - b) cell and tissue integrity
 - d) circulation of leukocytes (white blood cells)
 - e) organ formation during development
4. The extracellular matrix
 - a) exists around all eukaryotic cells
 - b) Is of cellular origin
 - e) Is basically made up of a combination of fibrous protein molecules and highly hydrated carbohydrate molecules.
5. The extracellular matrix is composed of
 - a) glycosaminoglycans
 - b) proteoglycans
 - d) fibrous proteins
6. Among the constituents of the extracellular matrix
 - a) Proteoglycans are associations of glycosaminoglycans covalently linked to a core protein.
 - b) Glycosaminoglycans are made up of repetitively associated dimers.
 - d) Collagen is a fibrous molecule rich in the amino acid hydroxyproline.
 - e) Laminin enables specific cell attachments.
7. Among the roles of the extracellular matrix, we can mention the following
 - a) resistance to crushing (compression resistance)
 - b) Cell attachment support
 - c) Support for cell migration
 - d) Survival signal via adhesion molecules
 - e) As a filter for molecules in the cellular environment
8. Collagen
 - a) Represents a family of matrix proteins.
 - b) Is the major constituent of the extracellular matrix.
 - c) Provides resistance to tensile forces.
 - d) Is consolidated by covalent bonds when fibrillar.
9. Cytoskeletal elements
 - a) Are protein polymers.
 - c) Ensure the cell's overall shape.
 - e) In the case of microtubules, can be involved in the intracellular movement of organelles.

10. Actin

- e) Polymerizes into filaments exhibiting dynamic instability at their ends in vivo

11. Concerning muscle fibers

- a) striated muscle comprises numerous bundles of muscle fibers
- c) each muscle fiber has contractile elements called myofibrils
- d) a myofibril is composed of several adjacent sarcomeres

12. Striated muscle contraction

- a) Requires the presence of actin and myosin
- c) Involves shortening of sarcomeres
- e) Results in actin filaments sliding over myosin filaments

13. Concerning sarcomeres

- b) A sarcomere is delimited by two Z striae
- d) Myosin heads possess ATPase activity
- e) sarcomere contraction requires the presence of Ca^{2+} .

14. About mitochondria

- c) The Krebs cycle produces NADH, ATP and CO_2

15. Mitochondria

- b) ATP synthetase is a biomolecular motor.
- c) Mitochondria contain DNA and ribosomes.
- e) Myopathies can be associated with mitochondrial dysfunction.

16. The mitochondrion

- a) Contains in its matrix the equipment necessary for protein synthesis
- b) Contains circular DNA

17. The mitochondrial inner membrane is characterized by

- a) Numerous ridges.
- c) High concentration of ATP synthetase.
- d) High concentration of cardiolipin and phosphatidylcholine. (Cardiolipin is a key lipid of the inner membrane.)

18. A nucleotide sequence is translated when it is in the form of

- d) mRNA

19. Ribosomal RNA (rRNA)

- b) are used for translation (They form the catalytic core of the ribosome.)
- c) associate with ribosomal proteins to form ribosomes
- d) are partially transcribed in the nucleolus

20. The amino acid sequence of a protein

- a) Is determined by the nucleotide sequence of its messenger RNA
- b) Is determined by the nucleotide sequence of its coding gene
- c) Strongly influences its shape (folding) and function
- d) Constitutes the primary structure

21. Translation

- b) requires messenger RNA (mRNA) and ribosomes

- c) requires the availability of amino acids (provided by transfer RNA)
22. Protein synthesis
- e) Requires the presence of transfer RNA
23. Golgi apparatus
- c) Involved in post-translational protein maturation.
 - d) Has numerous enzymes acting sequentially in deglycosylation and (re)glycosylation steps.
24. Lysosomes
- d) Contain hydrolytic enzymes
25. Lysosomes
- c) Use microtubular networks to move around the cell
 - d) are the destination of mannose-6 phosphate-tagged proteins from the Golgi apparatus
 - e) Contain a proton pump (ATPase H⁺ type V)

Exercise 2: Label and order the following diagrams:

The diagrams illustrate the process of translation, or protein synthesis, which is the process of synthesizing a protein from an mRNA template. The correct order of the diagrams is C, A, B.

Step 1: Initiation (Diagram C)

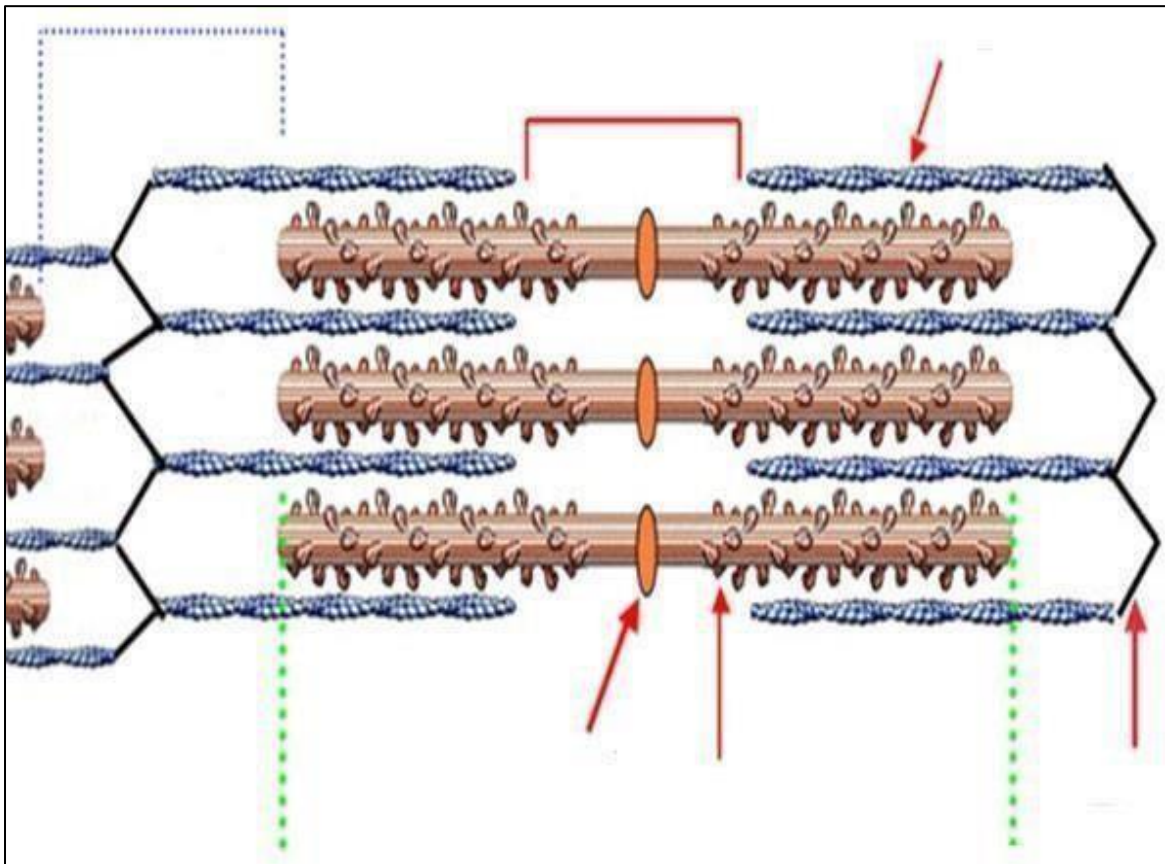
Step 2: Elongation (Diagram A)

Step 3: Termination (Diagram B)

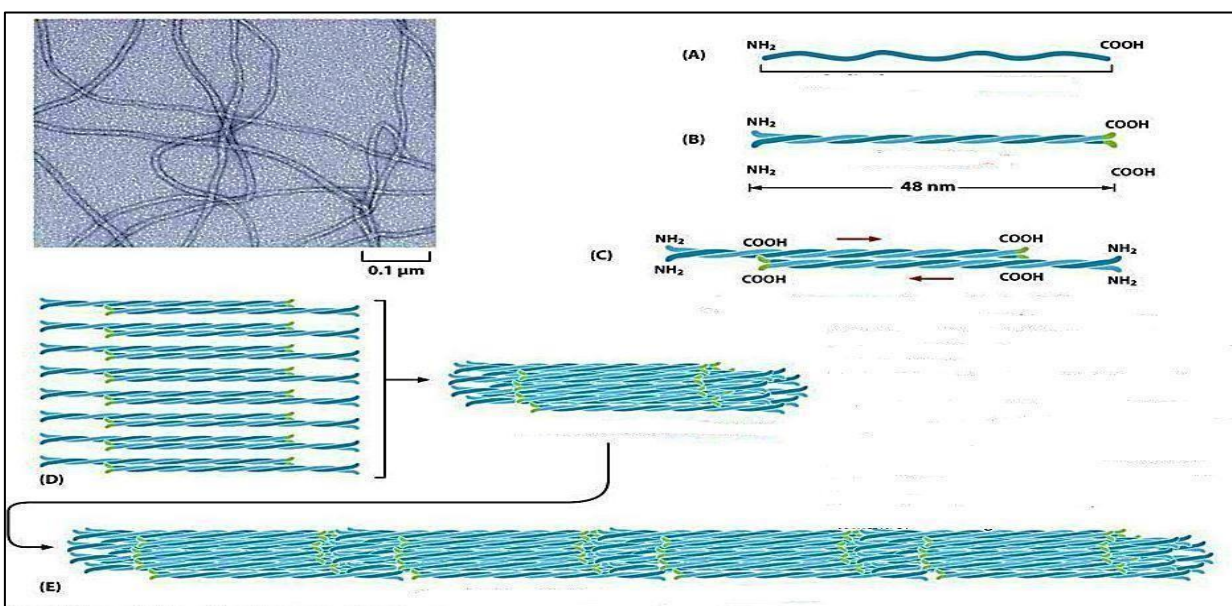
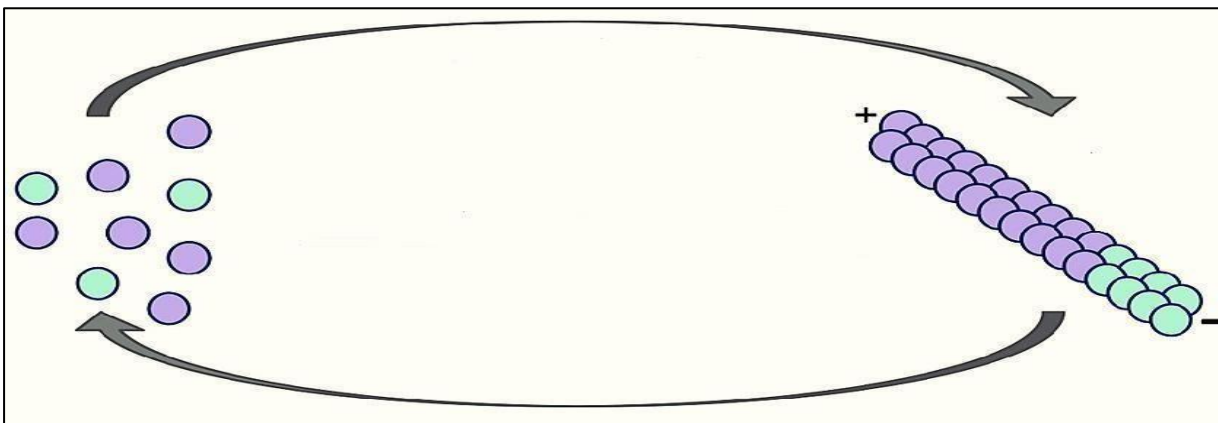
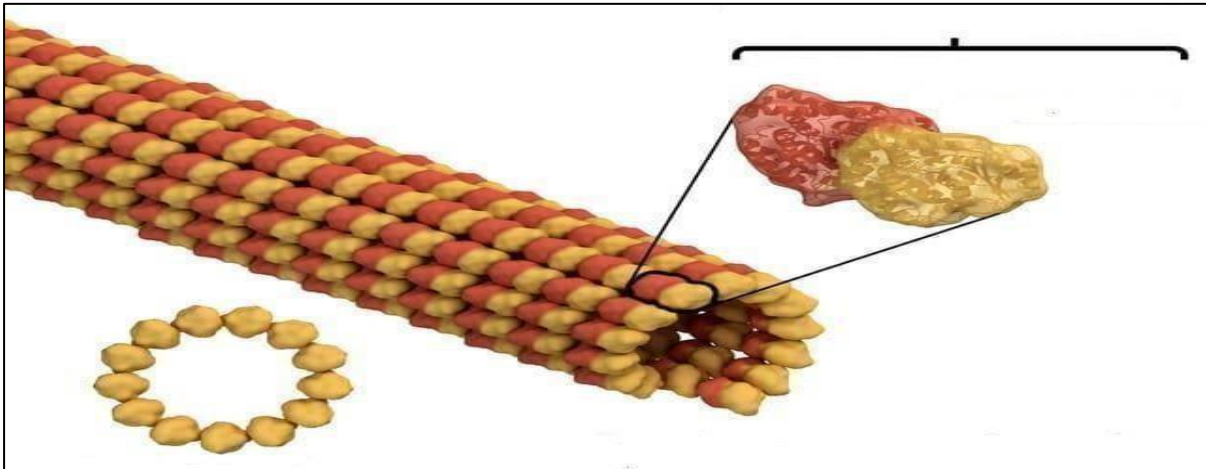
Tutorial N° 4

Exercise 1: Consider the figure below:

1. Name the structure in Figure below and fill in the blanks.
2. Name the type of cell that has this type of structure.
3. Give a definition of sarcomere.



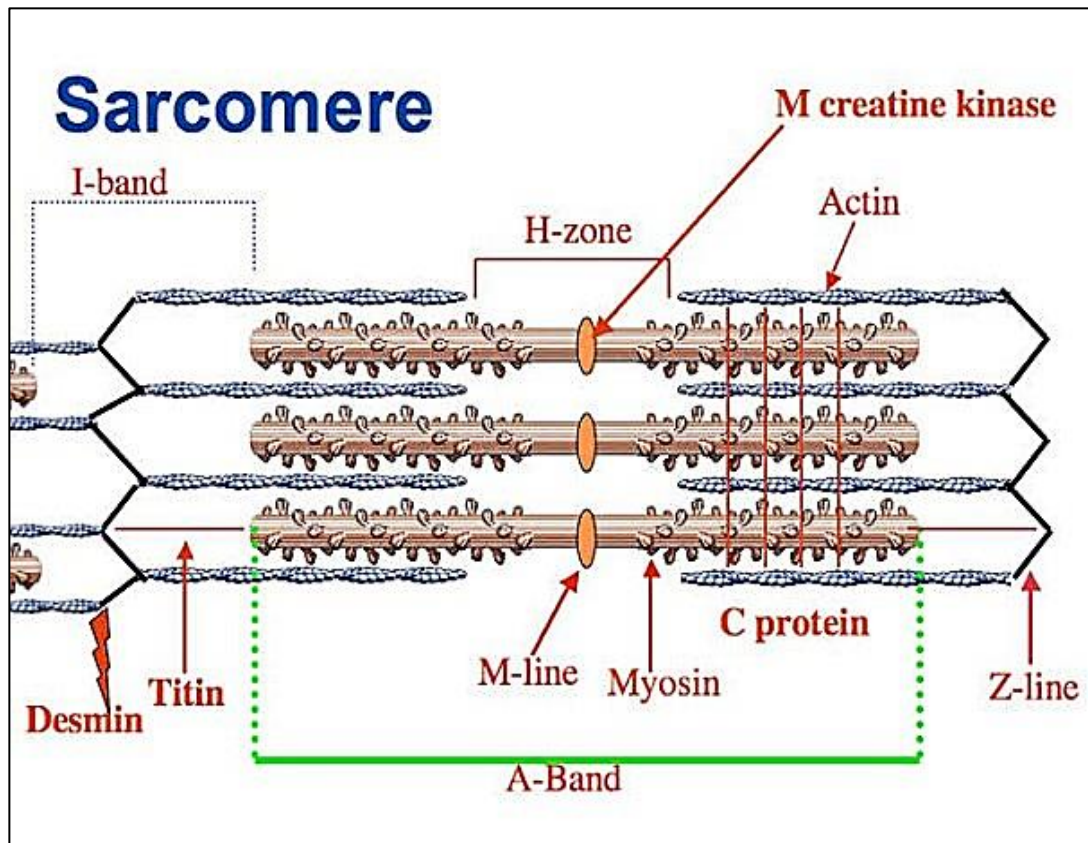
Exercise 3: Label and order the following diagrams:



Tutorial N° 4-Correction

Exercise 1

1. Name the structure in Figure below and fill in the blanks.



2. Name the type of cell that has this type of structure.

The type of cell that has this structure is a **muscle cell** or **myocyte**, specifically in striated muscle tissue (skeletal and cardiac muscle).

3. Definition

A sarcomere is the smallest functional unit of striated muscle tissue. It is the repeating unit between two Z-lines, composed of thick (myosin) and thin (actin) protein filaments. The sliding of these filaments past each other is responsible for muscle contraction.

Exercise 2: Label and order the following diagrams:

1. The blanks in the figures represent the different stages of intermediate filament assembly:

- (A) **Monomer**
- (B) **Coiled-coil dimer**
- (C) **Staggered tetramer**
- (D) **Eight tetramers packed into a helical array**
- (E) **Intermediate filament**

2. **Assembly of an Intermediate Filament**

Step 1: Identify the basic building blocks

The figure shows the hierarchical assembly of an intermediate filament. The basic building blocks are fibrous protein monomers, each with a central α - helical region.

Step 2: Describe the dimerization

In figure (A), two monomers associate to form a coiled-coil dimer. The N-terminus and C-terminus are at opposite ends, making the dimer a parallel structure.

Step 3: Describe the formation of the tetramer

In figure (B), two coiled-coil dimers associate in a staggered, antiparallel fashion to form a tetramer. This arrangement means the two ends of the tetramer are identical, making the structure nonpolar.

Step 4: Describe the final filament assembly

In figures (D) and (E), multiple tetramers associate both laterally and end-to-end to form the final rope-like intermediate filament. The final filament is approximately 10 nm in diameter and is a very stable structure.

Tutorial N° 5

Exercise

A. Glycoproteins: Types of Bonds and Interest in Glycosylation

1. Define glycosylation.
2. Distinguish between a glycoprotein and a glycolipid.
3. Name the two main types of protein glycosylation based on the bond between the protein and the glycan.

B. N-Glycosylation

4. Describe the two-step process of N-glycosylation.
5. In which cellular compartments does N-glycosylation and its subsequent remodeling occur?

C. Benefits of Glycosylation

6. List at least five biological roles or benefits of glycosylation.

Tutorial N° 5-Correction

A. Glycoproteins: Types of Bonds and Interest in Glycosylation

1. Define glycosylation.

Glycosylation is a fundamental co-translational and post-translational modification process where a carbohydrate chain, called a glycan, is enzymatically attached to a target molecule, such as a protein or lipid.

2. Distinguish between a glycoprotein and a glycolipid.

- **Glycoprotein:** A molecule consisting of a protein covalently bonded to one or more carbohydrate chains (glycans).
- **Glycolipid:** A molecule consisting of a lipid (e.g., ceramide) covalently bonded to one or more carbohydrate chains (glycans).

3. Name the two main types of protein glycosylation based on the bond between the protein and the glycan.

The two main types are:

1. **N-linked glycosylation** (Glycan attached to a Nitrogen atom)
2. **O-linked glycosylation** (Glycan attached to an Oxygen atom)

B. N-Glycosylation

4. Describe the two-step process of N-glycosylation.

1) **Synthesis of the Core Oligosaccharide:** A 14-sugar core oligosaccharide is assembled on a lipid carrier on the cytosolic face of the Endoplasmic Reticulum (ER). This core is then flipped into the ER lumen.

2) **En bloc Transfer and Trimming:** The entire pre-formed core oligosaccharide is transferred *en bloc* to a specific asparagine residue within the consensus sequence of a growing polypeptide chain. Immediately after transfer, the three glucose residues and one specific mannose residue are enzymatically removed as a quality control step in the ER.

5. In which cellular compartments does N-glycosylation and its subsequent remodeling occur?

- Initial Glycosylation and Core Trimming: Endoplasmic Reticulum (ER)
- Subsequent Remodeling and Maturation: Golgi Apparatus

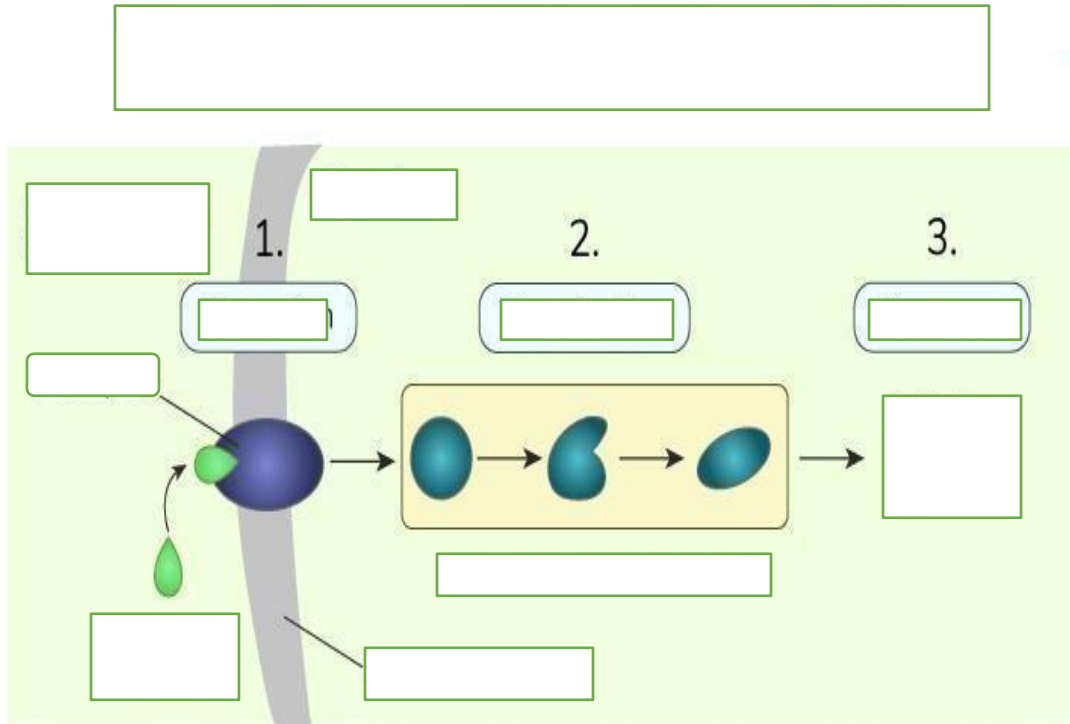
D. Benefits of Glycosylation

Glycosylation is crucial for a vast array of biological functions. Here are five key roles:

- 1) **Protein Folding and Stability:** Glycans in the ER help guide the correct folding of nascent proteins and prevent protein aggregation.
- 2) **Cell-Cell Recognition and Adhesion:** Glycans on the cell surface act as "identity tags," mediating interactions between cells (e.g., in immune recognition) and with the extracellular matrix.
- 3) **Protection from Proteolysis:** The bulky, hydrophilic glycan chains can shield the protein backbone from being degraded by proteolytic enzymes.
- 4) **Intracellular Trafficking:** Glycans serve as sorting signals that direct proteins to their correct cellular destinations (e.g., lysosomes, plasma membrane).
- 5) **Immune Response:** Glycans are critical for the function of antibodies and are recognized by specific immune cells. Aberrant glycosylation is often a hallmark of cancer and autoimmune diseases.
- 6) **Receptor Function:** Glycans can directly participate in ligand binding or modulate the activity of cell surface receptors.

Tutorial N° 6

Exercise 1: Provide a legend and title for the figure below:



Exercise 2

1. General Concepts of Cell Signaling

1. Define cellular communication.
2. List and describe the four main modes of cell signaling, including an example for each.

2. Ligands

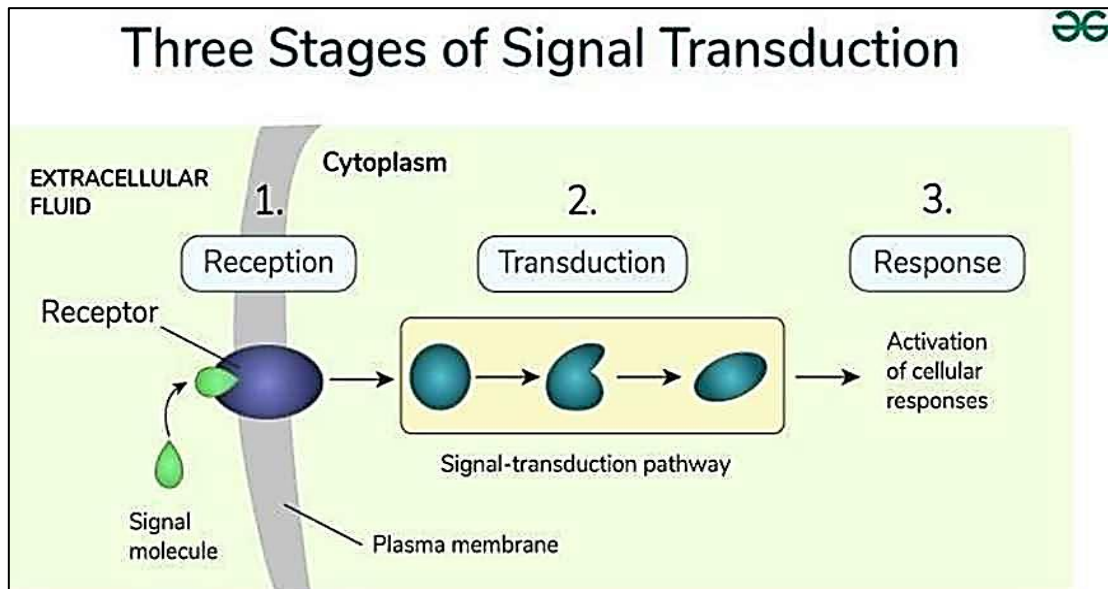
3. Differentiate between an agonist and an antagonist. Provide a pharmacological example of an antagonist.

3. Receptors - General Properties and Classification

4. List and explain the four main characteristics of receptors.
5. What are the two main classes of receptors based on their cellular location?

Tutorial N° 6- Correction

Exercise 1: Provide a legend and title for the figure below:



Exercise 2:

1) General Concepts of Cell Signaling

1. Define cellular communication.

Cellular communication is the process by which cells detect and respond to signals from their external environment (e.g., hormones, neurotransmitters) or from neighboring cells. This allows cells to coordinate their activities, ensuring the proper functioning of tissues, organs, and the entire organism.

2. List and describe the four main modes of cell signaling, including an example for each.

1. **Endocrine Signaling:** Hormones are released by endocrine glands into the bloodstream, which carries them to distant target cells.
2. **Paracrine Signaling:** Signaling molecules are released by a cell and act on nearby target cells in the local environment.
3. **Autocrine Signaling:** A cell secretes a signaling molecule that binds to receptors on its own surface, affecting itself.
4. **Direct Contact (Juxtacrine) Signaling:** Communication occurs through direct physical contact between the signaling and target cell. This can be via gap junctions (allowing direct passage of ions/small molecules) or interaction between surface proteins on two adjacent cells.

2) Ligands

3. Differentiate between an agonist and an antagonist. Provide a pharmacological example of an antagonist and its use.

- **Agonist:** A molecule that mimics the action of the natural ligand by binding to the receptor and *activating* it, producing a biological response.
- **Antagonist:** A molecule that binds to the receptor but does *not* activate it. Instead, it blocks the receptor, preventing the natural ligand or agonist from binding and producing a response.

3) Receptors - General Properties and Classification

4. List and explain the four main characteristics of receptors.

1. **Specificity:** A receptor typically binds only to one type of ligand or a closely related family of ligands, due to a complementary binding site. This ensures that only the correct signal elicits a response.
2. **Affinity:** The strength with which a receptor binds to its ligand. Receptors with high affinity can bind their ligand even when the ligand concentration is very low.
3. **Saturability:** Because the number of receptors on a cell is finite, the binding of ligands can be saturated. Once all receptors are occupied, increasing the ligand concentration will not increase the response.
4. **Reversibility:** Ligand-receptor binding is typically reversible. The ligand binds non-covalently and can dissociate, allowing the receptor to return to its inactive state and be ready for another signaling event.

5. What are the two main classes of receptors based on their cellular location?

1. **Intracellular Receptors:** Located inside the cell, in the cytoplasm or nucleus. Their ligands are typically small, hydrophobic (lipophilic) molecules that can diffuse across the plasma membrane.
2. **Cell-Surface Receptors (Transmembrane Receptors):** Span the plasma membrane. Their ligands are typically water-soluble (hydrophilic) molecules that cannot cross the membrane (e.g., insulin, adrenaline, growth factors).

Tutorial N° 7

Exercise: Select the appropriate one

1. The interaction of a hormone with its receptors:

- a) Is irreversible
- b) Is saturable
- c) Is specific
- d) Is necessarily a protein-protein interaction
- e) Always occurs at the plasma membrane

2. Regarding the phosphorylation reaction, it can be said that it is:

- a) The transfer of a phosphate group onto a molecule
- b) A covalent modification of a molecule
- c) Specific to proteins
- d) Irreversible
- e) A post-translational modification when performed on a protein

3. Protein phosphorylation

- a) Is done by a GTPase
- b) Is done by a kinase
- c) Consists of adding a phosphate to an amino acid (often serine, threonine, or tyrosine)
- d) Changes the protein's conformation, followed by a change in its activity
- e) Consists of adding GTP bound in a non-covalent manner

4. Plasma membrane receptors

- a) Associate with extracellular ligands in an irreversible manner.
- b) Generate intracellular signals involving "second messengers".
- c) Are only associated with G proteins.
- d) Are responsible for transducing information.
- e) Can be enzymes.

5. Regarding signal transduction:

- a) It is carried out by membrane receptors
- b) It amplifies an extracellular signal within the cell
- c) The binding of a first messenger to the receptor can be translated into various intracellular responses
- d) Protein kinase activity always leads to phosphorylations on serines or threonines
- e) Heterotrimeric GTPases are involved in the production of the second messenger cAMP

6. In multicellular organisms, the transduction of an extracellular signal can be ensured via:

- a) Gap junctions
- b) Membrane receptors
- c) Adenylyl cyclase
- d) Tubulin
- e) Phospholipase C

7. The transduction of an extracellular signal involving adenylyl cyclase occurs through several steps:

1. Hydrolysis of GTP to GDP by G proteins
2. Binding of the chemical mediator (ligand) to its specific receptor and conformational change of the receptor
3. Hydrolysis of ATP and cyclization of AMP by adenylyl cyclase
4. Replacement of GDP by GTP on the G protein (exchange)
5. Formation of the G protein-adenylyl cyclase complex
6. Activation of a phosphorylation cascade

In what chronological order do the different steps occur?

- a) 1,2,5,3,6,4
- b) 2,1,5,3,6,4
- c) 2,1,5,3,4,6
- d) 2,4,6,3,1,5
- e) 2,4,5,3,6,1

8. Receptors

- a) Are only expressed on the cell surface
- b) Allow intercellular communication
- c) Bind ligands such as steroid hormones, neurotransmitters, or growth factors
- d) Have a very weak interaction with their ligand
- e) Can possess catalytic activity

9. The nicotinic acetylcholine receptor:

- a) Is located at the neuromuscular junction.
- b) Is a Na⁺ and K⁺ channel.
- c) Activates a heterotrimeric G protein.
- d) Induces rapid contraction of skeletal muscles.
- e) Has a high affinity for its ligand acetylcholine.

10. The neuromuscular junction and muscle contraction

- a) Acetylcholine, the neurotransmitter of the neuromuscular junction, has a very high affinity for its receptors.
- b) Nicotinic-type cholinergic receptors allow the entry of sodium and the exit of potassium in the myocyte.
- c) Acetylcholine is degraded by acetylcholinesterase located in the synaptic cleft.
- d) The muscle action potential allows the re-release of calcium contained in the myocyte's mitochondria.
- e) At the sarcomere level, contraction is achieved by the sliding of actin filaments over myosin filaments without a change in the length of these two types of filaments.

11. Growth factor receptors with tyrosine kinase activity:

- a) Are proteins that cross the membrane four times
- b) Are activated by dimerization upon binding their ligand
- c) Can form signaling complexes with several effectors
- d) Are internalized and directed to peroxisomes
- e) Form weak interactions with their ligand

Tutorial N°7- Correction

Exercise: Here are the correct answers for each question.

1. b) Is saturable, c) Is specific
2. a) The transfer of a phosphate group onto a molecule, b) A covalent modification of a molecule, e) A post-translational modification when performed on a protein
3. b) Is done by a kinase, c) Consists of adding a phosphate to an amino acid (often serine, threonine, or tyrosine), d) Changes the protein's conformation, followed by a change in its activity
4. b) Generate intracellular signals involving "second messengers", d) Are responsible for transducing information., e) Can be enzymes.
5. a) It is carried out by membrane receptors, b) It amplifies an extracellular signal within the cell, c) The binding of a first messenger to the receptor can be translated into various intracellular responses, e) Heterotrimeric GTPases are involved in the production of the second messenger cAMP
6. a) Gap junctions, b) Membrane receptors, c) Adenylyl cyclase, e) Phospholipase C
7. e) 2,4,5,3,6,1
8. b) Allow intercellular communication, c) Bind ligands such as steroid hormones, neurotransmitters, or growth factors, e) Can possess catalytic activity
9. a) Is located at the neuromuscular junction., b) Is a Na⁺ and K⁺ channel., d) Induces rapid contraction of skeletal muscles., e) Has a high affinity for its ligand acetylcholine.
10. c) Acetylcholine is degraded by acetylcholinesterase located in the synaptic cleft., e) At the sarcomere level, contraction is achieved by the sliding of actin filaments over myosin filaments without a change in the length of these two types of filaments.
11. b) Are activated by dimerization upon binding their ligand, c) Can form signaling complexes with several effectors

Tutorial N° 8

The tutorial for this final chapter, entitled "**Signaling Abnormality and Pathology**," will be conducted as a series of oral presentations. Students, divided into groups, will be assigned one of the following topics:

- 1. RAS Proteins: Key Proto-Oncogenes in Tumorigenesis**
- 2. EGFR: From Tyrosine Kinase Receptor to Oncogene**
- 3. Mechanisms of Abnormal EGFR Activation and Therapeutic Implications**
- 4. KRAS: A Prevalent Oncogene and its Clinical Impact**
- 5. The RAS/MAPK Pathway: A Dysregulated Signaling Cascade in Cancer**
- 6. Oncogenes and Proto-oncogenes: How a Mutation Transforms a Normal Cell into a Cancer Cell**

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