1. (a) Give the function of the following: (1x5=5)
    - (i) Plasmodesmata
        - Function as channels that connect the cytoplasm of adjacent plant cells, allowing for the direct transport of water, nutrients, and signaling molecules between them.
    - (ii) Flippase
        - An enzyme that facilitates the ATP-dependent movement of specific phospholipids from one leaflet of a lipid bilayer to the other, helping to establish and maintain membrane asymmetry.
    - (iii) Lamins
        - Provide structural support to the nuclear envelope and are involved in various nuclear processes such as DNA replication, transcription, and chromatin organization.
    - (iv) Liposomes
        - Spherical vesicles composed of a lipid bilayer, used as models for cell membranes, and for drug delivery systems due to their ability to encapsulate both hydrophilic and hydrophobic substances.
    - (v) Aquaporins
        - Membrane proteins that form channels facilitating the rapid and selective passage of water molecules across cell membranes, playing a crucial role in maintaining cellular water balance.

(b) Give the contribution of ANY FIVE of the following scientists: (1x5=5)

- (i) Benda
    - Carl Benda is credited with coining the term "mitochondria" and for his early work in visualizing and describing these organelles.

- (ii) Peter Mitchell
  - Proposed the chemiosmotic hypothesis, explaining how ATP is generated in mitochondria and chloroplasts through a proton gradient across the membrane.
- (iii) Blobel & Sabatini
  - Developed the signal hypothesis, explaining how proteins are targeted to the endoplasmic reticulum and other organelles for secretion or insertion into membranes.
- (iv) Christian de Duve
  - Discovered lysosomes and peroxisomes, and significantly contributed to the understanding of their functions in cellular processes.
- (v) Tim Hunt, Paul Nurse, Lee Hartwell
  - Awarded the Nobel Prize for their discoveries concerning the key regulators of the cell cycle (cyclins and cyclin-dependent kinases).
- (vi) Lynn Margulis
  - Developed and popularized the endosymbiotic theory, which explains the origin of mitochondria and chloroplasts in eukaryotic cells.

(c) Expand ANY FIVE of the following: (1x5=5)

- (i) GPCR
  - G Protein-Coupled Receptor
- (ii) MTOC
  - Microtubule-Organizing Center
- (iii) GERL

- Golgi-Endoplasmic Reticulum-Lysosome

- (iv) CFTR
  - Cystic Fibrosis Transmembrane Conductance Regulator
- (v) cAMP
  - Cyclic Adenosine Monophosphate
- (vi) ATP
  - Adenosine Triphosphate

2. Distinguish between ANY FIVE of the following: (1x5=5)
   - (a) Microfilaments and Microtubules
     - **Microfilaments:** These are thin, flexible protein filaments composed primarily of actin, involved in cell shape, muscle contraction, and cell motility.
     - **Microtubules:** These are hollow, rigid cylinders made of tubulin protein, involved in maintaining cell shape, intracellular transport, and forming cilia, flagella, and spindle fibers during cell division.
   - (b) Mitosis and Meiosis
     - **Mitosis:** A type of cell division that results in two daughter cells each having the same number and kind of chromosomes as the parent nucleus, typically for growth and repair.
     - **Meiosis:** A type of cell division that results in four daughter cells each with half the number of chromosomes of the parent cell, as in the production of gametes and plant spores.
   - (c) Integral and Peripheral Proteins
     - **Integral Proteins:** Proteins that are permanently embedded within the lipid bilayer of the cell membrane, often spanning the entire membrane.

- **Peripheral Proteins:** Proteins that are temporarily associated with the lipid bilayer or with integral proteins on one side of the membrane, without penetrating the hydrophobic core.

- (d) Euchromatin and Heterochromatin
  - **Euchromatin:** Loosely packed, transcriptionally active form of chromatin, rich in genes and often undergoing transcription.
  - **Heterochromatin:** Tightly packed, transcriptionally inactive form of chromatin, generally found at the periphery of the nucleus or centromeres.
- (e) Tight junctions and Gap junctions
  - **Tight junctions:** Cell junctions that create a tight seal between adjacent cells, preventing the passage of molecules through the intercellular space and maintaining cell polarity.
  - **Gap junctions:** Cell junctions that form channels between adjacent animal cells, allowing for direct communication and the passage of small molecules and ions between their cytoplasms.
- (f) Dyneins and Kinesins
  - **Dyneins:** Motor proteins that move along microtubules, typically towards the minus end of the microtubule, involved in intracellular transport of vesicles and organelles, and in the movement of cilia and flagella.
  - **Kinesins:** Motor proteins that move along microtubules, typically towards the plus end of the microtubule, involved in intracellular transport of vesicles and organelles, and in chromosome movement during cell division.

3. What is oxidative phosphorylation? Describe how the Electron Transport Chain and ATP Synthase in the mitochondria help generate ATP-the energy currency of the cell. (15)

Oxidative phosphorylation is the metabolic pathway in which cells use enzymes to oxidize nutrients, thereby releasing energy which is used to reform ATP. In eukaryotes, this takes place in the mitochondria. It is the primary method of ATP production in aerobic organisms.

The process involves two main components: the Electron Transport Chain (ETC) and ATP Synthase.

- **Electron Transport Chain (ETC):**
  - The ETC is a series of protein complexes and electron carriers embedded in the inner mitochondrial membrane.
  - Electrons, derived from the oxidation of glucose and other fuel molecules (via NADH and FADH2 produced in glycolysis and the Krebs cycle), are passed sequentially from one carrier to the next in the ETC.
  - As electrons move down the chain, they release energy. This energy is used to pump protons (H+) from the mitochondrial matrix across the inner mitochondrial membrane into the intermembrane space.
  - This pumping action creates an electrochemical proton gradient, with a higher concentration of protons in the intermembrane space and a lower concentration in the matrix. This gradient is also known as the proton-motive force.
  - At the end of the ETC, oxygen acts as the final electron acceptor, combining with electrons and protons to form water. Without oxygen, the ETC would halt, and ATP production would cease.
- **ATP Synthase:**
  - ATP synthase is a large enzyme complex also embedded in the inner mitochondrial membrane.

- The proton gradient established by the ETC represents stored potential energy.
- Protons, driven by their electrochemical gradient, flow back from the intermembrane space into the mitochondrial matrix through a channel within the ATP synthase complex.
- The flow of protons causes a rotation of a part of the ATP synthase enzyme (the F0 rotor), which in turn drives conformational changes in another part (the F1 head).
- These conformational changes enable the F1 head to catalyze the phosphorylation of ADP (adenosine diphosphate) by inorganic phosphate (Pi) to produce ATP (adenosine triphosphate). This process is known as chemiosmosis.
- Thus, the energy released from the flow of protons down their concentration gradient is harnessed by ATP synthase to synthesize ATP.

In summary, the ETC uses the energy from electron transfer to pump protons, creating a gradient. ATP synthase then utilizes the energy of this proton gradient to drive the synthesis of ATP, effectively converting the energy stored in the proton-motive force into the chemical energy of ATP, the primary energy currency of the cell.

4. (a) Illustrate the process of microtubule assembly with the help of suitable diagram. Add a note on their role in cellular mobility. (7+3=10)

Process of Microtubule Assembly:

Microtubule assembly is a dynamic process involving the polymerization of tubulin dimers.

- **Tubulin Dimers:** Microtubules are composed of α-tubulin and β-tubulin subunits, which associate non-covalently to form an αβ-tubulin dimer. Each tubulin subunit binds to one molecule of GTP (guanosine triphosphate).

- **Nucleation:** The assembly process typically begins with a nucleation step, which is often facilitated by microtubule-organizing centers (MTOCs), such as the centrosome in animal cells. Within the MTOC, γ-tubulin ring complexes (γ-TuRCs) serve as templates for initiating microtubule growth.
- **Elongation:** Once nucleation has occurred, αβ-tubulin dimers add preferentially to the plus end of the growing microtubule. The β-tubulin subunit in the dimer hydrolyzes its bound GTP to GDP shortly after its incorporation into the microtubule.
- **GTP Cap:** Rapid growth at the plus end often results in a "GTP cap," where newly added dimers still contain GTP. This GTP cap stabilizes the microtubule.
- **Dynamic Instability:** Microtubules exhibit dynamic instability, meaning they can rapidly switch between phases of growth (polymerization) and shrinkage (depolymerization).
    - **Growth:** Occurs when the rate of tubulin addition to the plus end is faster than GTP hydrolysis, maintaining the GTP cap.
    - **Shrinkage (Catastrophe):** If the rate of GTP hydrolysis at the plus end outpaces the addition of new tubulin dimers, the GTP cap is lost, exposing GDP-bound tubulin. GDP-bound tubulin has a weaker affinity for neighboring tubulin molecules, leading to rapid depolymerization and microtubule shortening.
    - **Rescue:** Microtubules can switch back from shrinkage to growth, a process called rescue, usually by regaining a GTP cap.

Role in Cellular Mobility:

Microtubules play a crucial role in various forms of cellular mobility:

- **Intracellular Transport:** They serve as tracks for motor proteins (kinesins and dyneins) to transport vesicles, organelles, and

macromolecules throughout the cytoplasm. Kinesins generally move towards the plus end, while dyneins move towards the minus end.

- **Cilia and Flagella Movement:** Microtubules form the core structures (axonemes) of cilia and flagella. The coordinated sliding of microtubules, driven by dynein motor proteins, generates the beating movements necessary for cell locomotion (e.g., sperm, protozoa) or moving substances across cell surfaces (e.g., respiratory tract).
- **Chromosome Segregation:** During cell division (mitosis and meiosis), microtubules form the spindle fibers that are responsible for the precise segregation of chromosomes to daughter cells. Kinetochore microtubules attach to chromosomes, and polar and astral microtubules help organize the spindle and position the cell for division.
- **Cell Shape and Polarity:** Microtubules contribute to maintaining cell shape and establishing cell polarity, which is essential for directed cell migration and tissue organization.

(b) Discuss the role of secondary messengers in cell signaling. (5)

Secondary messengers are small, non-protein molecules or ions that relay signals from receptors on the cell surface to target molecules inside the cell. They act as intracellular mediators that amplify and diversify the initial signal received by a cell.

Their key roles in cell signaling include:

- **Signal Amplification:** A single activated receptor can trigger the production of many secondary messenger molecules, which in turn can activate many downstream target proteins. This allows a small initial signal to elicit a large cellular response.
- **Signal Transduction:** They bridge the gap between the activation of a receptor (often a G protein-coupled receptor or enzyme-linked receptor) at the plasma membrane and the activation of specific enzymes or other proteins within the cell.

- **Signal Diversity and Specificity:** Different secondary messengers activate different cellular pathways, allowing for diverse cellular responses to a variety of external stimuli. The specific combination and timing of secondary messenger production contribute to the specificity of the cellular response.
- **Rapid Diffusion:** Due to their small size, secondary messengers can diffuse rapidly throughout the cytoplasm, quickly distributing the signal to various cellular compartments and targets.
- **Regulation of Cellular Processes:** They regulate a wide array of cellular functions, including metabolism, gene expression, cell growth and division, secretion, and muscle contraction.
- **Examples:** Common secondary messengers include cyclic AMP (cAMP), cyclic GMP (cGMP), calcium ions (Ca^{2+}), inositol triphosphate (IP3), and diacylglycerol (DAG). Each of these activates specific downstream effectors to propagate the signal. For example, cAMP often activates protein kinase A (PKA), while Ca^{2+} can activate calmodulin and various protein kinases.

5. (a) What is Signal Hypothesis? How does vesicular transport take place from ER to Golgi apparatus? (5+5=10)

Signal Hypothesis:

The signal hypothesis, proposed by Günter Blobel and David Sabatini, explains how proteins destined for secretion, insertion into membranes, or delivery to certain organelles (like lysosomes) are targeted to the endoplasmic reticulum (ER).

- The hypothesis states that synthesis of these proteins begins on free ribosomes in the cytoplasm.
- A specific N-terminal amino acid sequence, called the "signal peptide" or "signal sequence," emerges first from the ribosome.
- This signal peptide is recognized by a Signal Recognition Particle (SRP), which temporarily halts translation.

- The SRP-ribosome-mRNA complex then binds to an SRP receptor on the ER membrane.
- Upon binding, translation resumes, and the ribosome docks onto a translocon (a protein channel) in the ER membrane.
- The polypeptide chain is then threaded through the translocon into the ER lumen (for soluble proteins) or inserted into the ER membrane (for transmembrane proteins), often with the help of chaperone proteins within the ER lumen.
- The signal peptide is typically cleaved off by a signal peptidase once the protein enters the ER lumen.
- This co-translational translocation ensures that proteins destined for the secretory pathway or certain organelles enter the ER as they are being synthesized.

Vesicular Transport from ER to Golgi Apparatus:

Vesicular transport is the primary mechanism by which proteins and lipids move from the ER to the Golgi apparatus. This process is essential for further processing, sorting, and delivery of these molecules.

- **Budding of COPII-coated Vesicles:** Proteins and lipids exiting the ER are packaged into small, spherical vesicles. This budding process is initiated by the assembly of a protein coat, specifically the COPII (Coat Protein Complex II) coat, on the ER membrane.
- **Cargo Selection:** Specific sorting signals on ER-resident proteins or proteins destined for the Golgi and beyond are recognized by cargo receptors embedded in the ER membrane. These receptors, along with adaptor proteins, recruit COPII coat proteins to form a bud.
- **Vesicle Formation:** As more COPII proteins assemble, they induce the curvature of the ER membrane, leading to the formation of a vesicle bud. This bud eventually pinches off from the ER, forming a free COPII-coated vesicle containing the cargo.

- **Uncoating:** Once the vesicle is released into the cytoplasm, the COPII coat rapidly disassembles (uncoats). This uncoating step is necessary for the vesicle to be able to fuse with its target membrane.
- **Movement to Golgi:** The uncoasted vesicles then move along microtubules, guided by motor proteins, towards the cis-Golgi network (the entry face of the Golgi apparatus).
- **Fusion with Golgi:** The vesicle docks at the cis-Golgi through specific SNARE (Soluble N-ethylmaleimide-sensitive factor attachment protein receptor) proteins on the vesicle (v-SNAREs) and the Golgi membrane (t-SNAREs). This interaction facilitates the fusion of the vesicle membrane with the cis-Golgi membrane, releasing the cargo into the Golgi lumen.
- **Retrograde Transport:** There is also a continuous retrograde transport from the Golgi back to the ER (mediated by COPI-coated vesicles) to retrieve ER-resident proteins that may have escaped and to recycle v-SNAREs and other components.

(b) Which organelle in the cell is also called the "Suicidal Bag". Enumerate its functions. (5)

The organelle in the cell that is also called the "Suicidal Bag" is the **Lysosome**.

Functions of Lysosomes:

- **Intracellular Digestion:** Lysosomes contain a variety of hydrolytic enzymes (e.g., proteases, lipases, nucleases, carbohydrases) that are active at an acidic pH (around 4.5-5.0). They are responsible for breaking down various macromolecules, including proteins, lipids, nucleic acids, and carbohydrates, that enter the cell through endocytosis (phagocytosis or pinocytosis) or autophagy.
- **Waste Disposal and Recycling:** They act as the cell's waste disposal system, digesting worn-out or damaged organelles (e.g., old mitochondria, ER fragments) and cellular debris through a process

called autophagy. The broken-down components can then be recycled back into the cytoplasm for new synthesis.

- **Pathogen Degradation:** In immune cells like macrophages, lysosomes play a crucial role in defending against pathogens. They fuse with phagosomes containing ingested bacteria or viruses, and their enzymes break down the invading microorganisms.
- **Programmed Cell Death (Apoptosis):** While not the primary trigger, the rupture of lysosomes and release of their enzymes into the cytoplasm can contribute to programmed cell death (apoptosis) in certain situations, hence the "suicidal bag" moniker.
- **Extracellular Digestion:** In some specialized cases, lysosomes can release their enzymes outside the cell to break down extracellular matrix components, for example, during bone resorption by osteoclasts.
- **Nutrient Release:** By breaking down complex molecules, lysosomes release smaller molecules (amino acids, sugars, fatty acids) that can be reused by the cell for energy or building blocks.

6. Write short notes on ANY THREE of the following: (5x3=15)
   - (a) Receptor-mediated endocytosis
     - Receptor-mediated endocytosis (RME), also known as clathrin-mediated endocytosis, is a highly specific and efficient process by which eukaryotic cells internalize specific macromolecules from the extracellular fluid. This process begins when specific ligands bind to complementary receptor proteins concentrated in specialized regions of the plasma membrane called clathrin-coated pits. Upon ligand binding, these pits invaginate and bud off from the plasma membrane, forming clathrin-coated vesicles. The clathrin coat then disassembles, and the uncoated vesicle, now an endosome, moves into the cytoplasm. The acidic environment of the endosome typically causes the dissociation of the ligand from its receptor. Receptors are often

recycled back to the plasma membrane, while the ligands are delivered to lysosomes for degradation or processed in other ways. This mechanism is crucial for the uptake of essential substances like cholesterol (via LDL receptors), iron (via transferrin receptors), and various hormones and growth factors, and also plays a role in signal transduction and pathogen entry.

- (b) Endosymbiotic Hypothesis
  - The Endosymbiotic Hypothesis, largely championed by Lynn Margulis, proposes that mitochondria and chloroplasts, key organelles in eukaryotic cells, originated from ancient prokaryotic cells that were engulfed by larger ancestral eukaryotic cells. According to this theory, a primitive anaerobic eukaryotic cell engulfed an aerobic bacterium, which, instead of being digested, established a symbiotic relationship, eventually evolving into mitochondria. Similarly, a later engulfment of a photosynthetic bacterium (like a cyanobacterium) by a eukaryotic cell containing mitochondria led to the evolution of chloroplasts. Evidence supporting this hypothesis includes the presence of their own circular DNA (similar to bacterial DNA), ribosomes (70S, like prokaryotes), and distinct double membranes (the inner membrane derived from the engulfed bacterium, and the outer from the host cell's phagosomal membrane). They also divide by binary fission, similar to bacteria, and their genetic sequences show clear relationships to bacterial counterparts. This hypothesis is fundamental to understanding the evolution of eukaryotic cells and the origin of cellular respiration and photosynthesis.

- (c) Cell Cycle checkpoints
  - Cell cycle checkpoints are critical regulatory mechanisms within the eukaryotic cell cycle that ensure the proper progression of events and maintain genomic integrity. These

checkpoints monitor for errors and ensure that each phase of the cell cycle is completed accurately before proceeding to the next. If problems are detected (e.g., DNA damage, incomplete DNA replication, improper chromosome alignment), the cell cycle can be temporarily arrested, allowing time for repairs or corrections. If the damage is irreparable, the checkpoints can trigger programmed cell death (apoptosis). Major checkpoints include:

- **G1 Checkpoint (Restriction Point):** Monitors for DNA damage, cell size, nutrient availability, and growth factors. It is the most important decision point where a cell commits to dividing or entering a quiescent G0 state.
- **G2 Checkpoint:** Ensures that DNA replication is complete and that there is no DNA damage before entering mitosis.
- **M Checkpoint (Spindle Assembly Checkpoint):** Occurs during metaphase and ensures that all chromosomes are correctly attached to the mitotic spindle microtubules and aligned at the metaphase plate before anaphase begins.

- These checkpoints involve a complex network of protein kinases (CDKs) and cyclins, along with various sensor, transducer, and effector proteins, which collectively regulate the progression of the cell cycle. Failures in checkpoint mechanisms can lead to genomic instability and are often implicated in cancer development.

- (d) Protein modifications in ER
  - The endoplasmic reticulum (ER) is a major site for the synthesis, folding, and modification of proteins destined for secretion, insertion into membranes, or delivery to organelles like the Golgi, lysosomes, and peroxisomes. As proteins enter

the ER lumen or membrane, they undergo several crucial modifications:

- **Signal Peptide Cleavage:** The N-terminal signal peptide, which targeted the protein to the ER, is often cleaved by signal peptidase.
- **Glycosylation:** Many proteins are N-linked glycosylated, meaning an oligosaccharide chain is added to an asparagine residue. This occurs cotranslationally and plays roles in protein folding, quality control, and cell-cell recognition. Further modifications to these oligosaccharides occur in the Golgi.
- **Disulfide Bond Formation:** Disulfide bonds (S-S bonds) are formed between cysteine residues, catalyzed by protein disulfide isomerase (PDI) in the oxidizing environment of the ER lumen. These bonds are crucial for the stability and proper folding of many secreted and membrane proteins.
- **Protein Folding and Quality Control:** Chaperone proteins like BiP (Binding immunoglobulin Protein) and calnexin/calreticulin assist in the correct folding of newly synthesized proteins. The ER also has a robust quality control system, retaining misfolded proteins for refolding or targeting them for degradation via ER-associated degradation (ERAD).
- **Assembly of Multi-subunit Proteins:** Multi-subunit proteins often assemble within the ER lumen before being transported to their final destination.
- **GPI Anchor Addition:** Some proteins receive a glycosylphosphatidylinositol (GPI) anchor, attaching them to the outer leaflet of the plasma membrane.

- These modifications are essential for the proper function, stability, and targeting of proteins within the secretory pathway.

- (e) Nuclear Pore Complex
  - The Nuclear Pore Complex (NPC) is a large, intricate protein assembly that spans the double membrane of the nuclear envelope, forming channels that regulate the transport of molecules between the nucleus and the cytoplasm. Eukaryotic cells contain thousands of NPCs, each composed of multiple copies of about 30 different proteins called nucleoporins (Nups).
  - **Structure:** The NPC has an octagonal symmetry and consists of several distinct structural components:
    - **Cylindrical Channel:** A central channel that allows for the passage of molecules.
    - **Cytoplasmic Filaments:** Extend into the cytoplasm, thought to be involved in initial recognition of cargo.
    - **Nuclear Basket:** A basket-like structure that extends into the nucleoplasm.
    - **Spokes and Rings:** Radial spokes connect the inner and outer rings, forming the main framework.
  - **Function:** NPCs are essential for:
    - **Selective Transport:** They mediate the selective active transport of large molecules (proteins and RNAs) into and out of the nucleus. This transport is signal-dependent, requiring specific nuclear localization signals (NLS) for import and nuclear export signals (NES) for export, which are recognized by transport receptors (importins and exportins).

- **Passive Diffusion:** Small molecules, ions, and proteins (typically < 30-60 kDa) can freely diffuse through the NPC channel, moving down their concentration gradients.
- **Regulation of Gene Expression:** By controlling the import of transcription factors and the export of various RNAs, NPCs play a critical role in regulating gene expression.

- The highly regulated transport through the NPC ensures that the unique environment of the nucleus is maintained and that nuclear processes like DNA replication and transcription are properly coordinated with cytoplasmic events.