1. **(a) Define the following (Any Four): (4×1=4)**

   - **(i) Yamanaka factors:**
     - Yamanaka factors are a specific set of four transcription factors: Oct3/4, Sox2, Klf4, and c-Myc.
     - They are collectively used to reprogram differentiated somatic cells (e.g., skin cells) into induced pluripotent stem cells (iPSCs).
     - These iPSCs have characteristics similar to embryonic stem cells, including the ability to differentiate into various cell types.
   - **(ii) Ribozyme:**
     - A ribozyme is an RNA molecule that possesses catalytic activity, similar to protein enzymes.
     - It can catalyze specific biochemical reactions, such as cleavage of phosphodiester bonds in other RNA molecules or in itself.
     - Examples include ribosomal RNA (rRNA) in peptide bond formation during translation and certain self-splicing introns.
   - **(iii) Silencer elements:**
     - Silencer elements are DNA sequences that bind to specific transcription factors called repressors.
     - When repressors bind to silencer elements, they decrease the rate of transcription of a gene.
     - They can act at considerable distances from the gene they regulate and can be located upstream, downstream, or within an intron.
   - **(iv) Central Dogma:**

Duhive

- The Central Dogma of molecular biology describes the fundamental flow of genetic information in biological systems.
- It states that genetic information flows generally from DNA to RNA to protein.
- While exceptions exist (e.g., reverse transcription), it remains a foundational concept in understanding gene expression.

- **(v) Split genes:**
  - Split genes are genes in eukaryotes that are interrupted by non-coding sequences called introns.
  - The coding regions, called exons, are separated by these introns.
  - During gene expression, the entire gene is transcribed into a primary RNA transcript, and then the introns are removed by a process called splicing to form the mature mRNA.

Duhive

2. **(b) Differentiate between (Any Three): (3×2=6)**
   - **(i) Euchromatin and Heterochromatin:**
     - **Euchromatin:**
       - Less condensed form of chromatin.
       - Transcriptionally active and gene-rich.
       - Undergoes active transcription, allowing genes to be expressed.
       - Stains lightly with DNA-binding dyes.
     - **Heterochromatin:**
       - Highly condensed form of chromatin.
       - Transcriptionally inactive or silenced and gene-poor.

- Contains repetitive DNA sequences and plays structural roles, such as in centromeres and telomeres.
- Stains darkly with DNA-binding dyes.

- **(ii) Apoptosis and Necrosis:**
  - **Apoptosis:**
    - Programmed cell death, an active and regulated process.
    - Often characterized by cell shrinkage, chromatin condensation, DNA fragmentation, and formation of apoptotic bodies.
    - Does not typically induce an inflammatory response.
    - Physiological role in development, tissue homeostasis, and elimination of damaged cells.
  - **Necrosis:**
    - Uncontrolled cell death, usually caused by external injury (e.g., toxins, trauma, infection).
    - Characterized by cell swelling, rupture of the plasma membrane, and leakage of cellular contents.
    - Induces a strong inflammatory response in surrounding tissues.
    - Always pathological.
- **(iii) Activators and Repressors:**
  - **Activators:**
    - Transcription factors that bind to specific DNA sequences (enhancers or promoter-proximal elements) and increase the rate of gene transcription.

Duhive

- They often recruit RNA polymerase or other components of the transcription machinery.
- Can interact with co-activators to further boost transcription.

▪ **Repressors:**

- Transcription factors that bind to specific DNA sequences (silencers or operator regions) and decrease or prevent the rate of gene transcription.
- They can block RNA polymerase binding, interfere with activator function, or recruit co-repressors that modify chromatin structure to make it less accessible.

○ **(iv) Totipotent and Pluripotent Stem cells:**

Duhive

▪ **Totipotent Stem Cells:**

- Have the highest differentiation potential.
- Can differentiate into all cell types, including the embryonic and extraembryonic tissues (like the placenta and umbilical cord).
- Only the zygote and the cells of the first few divisions (morula stage) are considered totipotent.

▪ **Pluripotent Stem Cells:**

- Can differentiate into all cell types that make up the three germ layers (ectoderm, mesoderm, endoderm) of the embryo.
- Cannot form extraembryonic tissues.
- Embryonic stem cells (ESCs) derived from the inner cell mass of the blastocyst and induced pluripotent stem cells (iPSCs) are examples.

3. **(c) Expand the following: (0.5×6=3)**
    - **(i) CPSF:** Cleavage and Polyadenylation Specificity Factor
    - **(ii) CREB:** cAMP Response Element-Binding protein
    - **(iii) NELF:** Negative Elongation Factor
    - **(iv) RNP:** Ribonucleoprotein
    - **(v) ORF:** Open Reading Frame
    - **(vi) CAP-cAMP:** Catabolite Activator Protein-cyclic Adenosine Monophosphate
4. **(d) State the reasons: (2×1=2)**
    - **(i) Why transcription occurs in 5' to 3' direction only?**
        - Transcription occurs in the 5' to 3' direction because RNA polymerase, like DNA polymerase, can only add new ribonucleotides to the 3'-hydroxyl ($3' - OH$) end of the growing RNA strand.
        - The enzyme moves along the DNA template strand in a 3' to 5' direction, synthesizing the RNA strand that is antiparallel and complementary to the template, thus extending the RNA in the 5' to 3' direction.
    - **(ii) Why primase is required for DNA replication but not for transcription?**
        - **Primase is required for DNA replication** because DNA polymerase cannot initiate DNA synthesis de novo (from scratch). It can only extend an existing nucleotide strand. Primase synthesizes a short RNA primer, which provides the necessary free 3'-hydroxyl group for DNA polymerase to begin adding deoxyribonucleotides.
        - **Primase is NOT required for transcription** because RNA polymerase (the enzyme responsible for transcription) *can*

Duhive

initiate RNA synthesis de novo. It does not need a pre-existing 3'-OH group to start building the RNA molecule from the DNA template.

2. **(a) Discuss the mechanism of DNA replication in a bacterial cell. (10)**

DNA replication in bacterial cells (prokaryotes) is a highly regulated and efficient process that results in the accurate duplication of the entire circular chromosome. It is a semi-conservative process, meaning each new DNA molecule consists of one original strand and one newly synthesized strand.

The mechanism can be divided into three main stages: initiation, elongation, and termination.

- **1. Initiation:**
    - **Origin of Replication (OriC):** Replication begins at a specific, AT-rich sequence on the bacterial chromosome called *oriC*. This region contains DnaA boxes, which are binding sites for the DnaA initiator protein, and DNA unwinding elements (DUEs).
    - **DnaA Binding and Unwinding:** Multiple copies of the DnaA protein bind to the DnaA boxes within *oriC*. This binding causes the DNA to wrap around the DnaA proteins, introducing strain that facilitates the unwinding of the adjacent AT-rich DUEs.
    - **Helicase Loading:** The unwound region allows for the loading of DnaB helicase (a hexameric protein), which is delivered to the origin by DnaC protein (a helicase loader). Helicase then binds to the single-stranded DNA and continues to unwind the DNA bidirectionally, creating two replication forks.
    - **Single-Stranded Binding Proteins (SSBs):** As the DNA unwinds, single-stranded binding proteins (SSBs) immediately bind to the separated single strands. This prevents the reannealing of the DNA strands and protects them from degradation.
    - **DNA Gyrase (Topoisomerase II):** As helicase unwinds the DNA, positive supercoiling builds up ahead of the replication forks. DNA

Duhive

gyrase (a type II topoisomerase) relieves this supercoiling by introducing transient double-strand breaks, passing DNA strands through the breaks, and then rejoining them, thus preventing the DNA from tangling and stalling replication.

- **2. Elongation:**
    - **Primer Synthesis by Primase:** DNA polymerase cannot initiate DNA synthesis. Therefore, an RNA polymerase called primase (a type of RNA polymerase that does not require a primer) synthesizes short RNA primers (5-10 nucleotides long) on both template strands. Each primer provides a free 3'-hydroxyl group for DNA polymerase to extend.
    - **Leading Strand Synthesis:**
        - On one template strand (the leading strand template), DNA synthesis occurs continuously in the 5' to 3' direction, following the movement of the replication fork.
        - Only one RNA primer is needed for the synthesis of the entire leading strand.
        - DNA Polymerase III (Pol III), the primary replicative polymerase in bacteria, extends this primer continuously.
    - **Lagging Strand Synthesis:**
        - The other template strand (the lagging strand template) is oriented in the 5' to 3' direction relative to the replication fork, meaning DNA synthesis must occur discontinuously, in short fragments.
        - These short fragments are called Okazaki fragments.
        - For each Okazaki fragment, primase synthesizes a new RNA primer.

Duhive

- DNA Polymerase III then extends this primer in the 5' to 3' direction until it encounters the previously synthesized Okazaki fragment.

- **Primer Removal and Gap Filling:**
  - Once DNA Pol III finishes an Okazaki fragment, DNA Polymerase I (Pol I) takes over.
  - Pol I possesses 5' to 3' exonuclease activity, which removes the RNA primers one nucleotide at a time.
  - Simultaneously, Pol I uses its 5' to 3' polymerase activity to fill in the gaps with deoxyribonucleotides.
- **Ligation:**
  - After Pol I removes the primer and fills the gap, a nick remains between the 3'-OH end of the newly synthesized DNA and the 5'-phosphate end of the adjacent Okazaki fragment.
  - DNA ligase seals this nick by forming a phosphodiester bond, using ATP or NAD^+ as an energy source.

Duhive

- **3. Termination:**
  - **Ter Sites:** In *E. coli*, replication forks meet at specific termination sequences called *Ter* sites (TerA to TerJ) located opposite to *oriC* on the circular chromosome.
  - **Tus Protein:** These *Ter* sites are bound by a protein called Tus (terminus utilization substance). The Tus-Ter complex acts as a "replication fork trap," allowing a replication fork to pass through in one direction but blocking the progression of a fork from the other direction.
  - **Decatenation:** Once the two replication forks meet and the entire chromosome is replicated, the two newly synthesized circular DNA molecules are interlinked (catenated).

- **Topoisomerase IV:** A type II topoisomerase, specifically Topoisomerase IV in bacteria, is required to decatenate these interlinked chromosomes, separating them into two individual, identical circular DNA molecules. These can then be segregated into daughter cells during cell division.

This well-orchestrated process ensures high fidelity and efficiency in transmitting genetic information from one generation to the next.

(b) Discuss the salient features of Genetic code. (5)

The genetic code is the set of rules by which information encoded in genetic material (DNA or RNA sequences) is translated into proteins (amino acid sequences) by living cells. It is fundamental to molecular biology and possesses several key features:

- **1. Triplet Code:**
  - The genetic code is read in groups of three nucleotide bases, called codons.
  - Each codon specifies a particular amino acid or a stop signal.
  - Since there are four types of bases (A, U, G, C in RNA), there are $4^3 = 64$ possible codons.
- **2. Degenerate (Redundant):**
  - The genetic code is degenerate, meaning that most amino acids are specified by more than one codon.
  - For example, both UUA and UUG code for Leucine.
  - This degeneracy often occurs at the third position of the codon (the "wobble position"), providing some flexibility and a buffer against point mutations.
- **3. Non-overlapping:**

Duhive

- The genetic code is non-overlapping, meaning that each nucleotide in an mRNA sequence is part of only one codon.
- After one codon is read, the next codon immediately follows it without sharing any nucleotides.
- For example, if the sequence is ABCDEF, it is read as ABC, then DEF, not ABC, BCD, CDE.

- **4. Commaless (No Punctuation within Genes):**
  - The genetic code is commaless, meaning there are no intervening nucleotides or "punctuation marks" between adjacent codons within the coding sequence of a gene.
  - The codons are read continuously in a sequential manner.
- **5. Universal (Nearly Universal):**
  - The genetic code is largely universal, meaning that the same codons specify the same amino acids in almost all living organisms, from bacteria to humans.
  - This universality suggests a common evolutionary origin of life.
  - However, there are a few minor exceptions, particularly in mitochondrial DNA and some single-celled organisms, where a few codons may specify different amino acids or stop signals.
- **6. Start Codon and Stop Codons:**
  - **Start Codon:** AUG is the most common start codon. It signals the beginning of protein synthesis and also codes for Methionine (Met) in eukaryotes and N-formylmethionine (fMet) in prokaryotes.
  - **Stop Codons (Nonsense Codons):** UAA, UAG, and UGA are the three stop codons. They do not code for any amino acid but signal the termination of protein synthesis.

Duhive

These features ensure the accurate and efficient translation of genetic information into functional proteins, which is essential for all cellular processes.

3. **(a) Define Apoptosis and write down its hallmark features. Explain the intrinsic pathway in regulation of apoptosis with the help of suitable examples. (10)**

Define Apoptosis:

Apoptosis is a highly regulated and controlled process of cell death, often referred to as "programmed cell death." It is an active and energy-dependent process that plays a critical role in development, tissue homeostasis, and the elimination of damaged, old, or potentially harmful cells without causing an inflammatory response in the surrounding tissue. It contrasts sharply with necrosis, which is uncontrolled and often results from acute injury.

Hallmark Features of Apoptosis:

Duhive

Apoptosis is characterized by a distinctive set of morphological and biochemical changes:

- **Cell Shrinkage:** The cell volume decreases, and the cell rounds up.
- **Chromatin Condensation:** Chromatin within the nucleus condenses and aggregates, often against the nuclear envelope.
- **Nuclear Fragmentation (Karyorrhexis):** The nucleus breaks down into several distinct fragments.
- **DNA Fragmentation:** The cell's DNA is cleaved into fragments of characteristic sizes (multiples of 180-200 base pairs) by specific endonucleases (e.g., CAD, Caspase-Activated DNase). This can be visualized as a "DNA ladder" on gel electrophoresis.
- **Membrane Blebbing:** The plasma membrane forms irregular protrusions or "blebs."

- **Formation of Apoptotic Bodies:** The cell breaks up into membrane-bound vesicles called apoptotic bodies, which contain cytoplasmic contents and nuclear fragments.
- **Phagocytosis:** Apoptotic bodies are rapidly recognized and engulfed by phagocytic cells (e.g., macrophages) without eliciting an inflammatory response.
- **Loss of Mitochondrial Membrane Potential:** Early in apoptosis, mitochondria often undergo changes, including the loss of their transmembrane potential.
- **Caspase Activation:** A central biochemical hallmark is the activation of a family of cysteine proteases called caspases, which act in a proteolytic cascade.

Intrinsic Pathway in Regulation of Apoptosis:

Duhive

The intrinsic (or mitochondrial) pathway of apoptosis is triggered by intracellular signals that result from cellular stress, DNA damage, growth factor withdrawal, or developmental cues. It is primarily controlled by the balance of pro-apoptotic and anti-apoptotic proteins of the Bcl-2 family, which ultimately regulate mitochondrial outer membrane permeabilization (MOMP).

Mechanism and Examples:

5. **Initiating Stimuli:** Various cellular stresses can trigger the intrinsic pathway:
    - **DNA damage:** Induced by radiation or chemotherapy agents.
    - **Growth factor withdrawal:** Cells that are dependent on specific growth factors will undergo apoptosis if these factors are removed.
    - **Hypoxia:** Lack of oxygen.
    - **Oxidative stress:** Accumulation of reactive oxygen species.
    - **ER stress:** Accumulation of misfolded proteins in the endoplasmic reticulum.

- **Cellular damage/dysfunction:** Unrepairable damage that signals the cell to self-destruct.

6. **Bcl-2 Family Proteins:** This family of proteins regulates the integrity of the mitochondrial outer membrane:
    - **Anti-apoptotic Bcl-2 proteins:** Bcl-2, Bcl-xL, Mcl-1. These proteins reside on the outer mitochondrial membrane and inhibit apoptosis by preventing MOMP.
    - **Pro-apoptotic effector Bcl-2 proteins:** Bax, Bak. These proteins can oligomerize and form pores in the mitochondrial outer membrane, leading to MOMP.
    - **Pro-apoptotic BH3-only proteins:** Bid, Bad, Bim, PUMA, Noxa. These proteins sense cellular stress and act as "sentinels." They activate Bax and Bak or directly inhibit the anti-apoptotic Bcl-2 proteins.
7. **Mitochondrial Outer Membrane Permeabilization (MOMP):**
    - Upon receiving an apoptotic signal (e.g., DNA damage), pro-apoptotic BH3-only proteins are activated.
    - They either directly activate Bax and Bak, or they bind to and neutralize the anti-apoptotic Bcl-2 proteins (like Bcl-2 and Bcl-xL), thus "releasing" Bax and Bak from inhibition.
    - Activated Bax and Bak then oligomerize and insert into the outer mitochondrial membrane, forming pores.
    - This leads to MOMP, which is the "point of no return" in the intrinsic pathway.
8. **Release of Pro-apoptotic Factors:**
    - MOMP allows the release of various pro-apoptotic proteins from the intermembrane space of the mitochondria into the cytosol.
    - The most critical of these is **Cytochrome c**.

Duhive

- Other released factors include Smac/Diablo (which neutralize IAPs - Inhibitors of Apoptosis Proteins) and Omi/HtrA2.

9. **Caspase Activation Cascade:**
    - Once in the cytosol, Cytochrome c binds to **Apaf-1 (Apoptotic Protease Activating Factor-1)**.
    - This complex then recruits and activates **Procaspase-9** (an initiator caspase) by facilitating its auto-cleavage.
    - The activated Apaf-1/cytochrome c/caspase-9 complex is called the **apoptosome**.
    - Activated Caspase-9 then cleaves and activates downstream **effector caspases** (e.g., Caspase-3, Caspase-6, Caspase-7).
    - These effector caspases are responsible for cleaving numerous cellular substrates, leading to the characteristic biochemical and morphological changes of apoptosis, such as DNA fragmentation (by activating CAD) and degradation of structural proteins.

Duhive

Example:

- **Cancer Therapy:** Many anti-cancer drugs, such as chemotherapeutic agents (e.g., cisplatin, etoposide) or radiation therapy, induce DNA damage in rapidly dividing cancer cells. This DNA damage activates stress-responsive proteins (e.g., p53), which in turn activate BH3-only proteins (like PUMA or Noxa). These BH3-only proteins then trigger the intrinsic apoptotic pathway by promoting MOMP and subsequent caspase activation, leading to the death of the cancerous cells.

In essence, the intrinsic pathway acts as an internal cell suicide program, triggered by various forms of cellular stress and orchestrated primarily by the Bcl-2 protein family and subsequent mitochondrial dysfunction and caspase activation.

(b) Design an experiment to prove that DNA replication is semi-conservative. (5)

The semi-conservative model of DNA replication states that each new DNA molecule consists of one original (parental) strand and one newly synthesized

(daughter) strand. This was elegantly proven by Meselson and Stahl in 1958 using density gradient centrifugation.

Experiment Design (Meselson-Stahl Experiment):

Aim: To determine the mode of DNA replication (conservative, semi-conservative, or dispersive).

Principle: The experiment relies on the ability to distinguish "old" DNA from "new" DNA based on their density, by incorporating different isotopes of nitrogen into the DNA.

- **Isotopes Used:**
    - ^{N}**N (heavy nitrogen):** A stable, non-radioactive isotope of nitrogen, which is denser than normal nitrogen.
    - ^{14}**N (light nitrogen):** The common, naturally occurring isotope of nitrogen.
- **Organism:** *Escherichia coli* (E. coli) bacteria are ideal due to their rapid growth and relatively simple DNA.
- **Procedure:**

  Step 1: Grow E. coli in ^{15}N Medium (for multiple generations).

    - Grow a culture of *E. coli* for many generations (e.g., 14-20 generations) in a growth medium where the only nitrogen source available is the heavy isotope, $^{15}NH_4Cl$.
    - **Expected Result:** After many generations, all the nitrogenous bases in the E. coli DNA will contain ^{15}N.
    - **Observation:** When DNA is extracted from these cells and subjected to cesium chloride (CsCl) density gradient centrifugation, it will form a single, heavy band at the bottom of the centrifuge tube. This "heavy" DNA serves as the starting reference.

  Step 2: Transfer E. coli to ^{14}N Medium (for one generation).

Duhive

- Take a sample of the ^{15}N-labeled *E. coli* cells and transfer them to a fresh growth medium where the only nitrogen source is the light isotope, $^{14}NH_4Cl$.
- Allow the cells to replicate their DNA only **once** (one generation).
- **Expected Result (based on semi-conservative model):** Each new DNA molecule should consist of one ^{15}N (original) strand and one ^{14}N (newly synthesized) strand. Therefore, the DNA should have an intermediate density.
- **Observation:** When DNA is extracted from these cells and centrifuged in CsCl, it will form a single band, but at an **intermediate density** position, precisely between the "heavy" (^{15}N-^{15}N) band and the "light" (^{14}N-^{14}N) band.

Step 3: Allow E. coli to Replicate in ^{14}N Medium (for a second generation).

Duhive

- Take a sample of the cells from Step 2 and allow them to replicate their DNA for **another generation** in the continuous presence of ^{14}N medium.
- **Expected Result (based on semi-conservative model):**
  - The hybrid DNA molecules from the first generation will each serve as templates.
  - Replication will produce two types of DNA molecules:
    - Half of the molecules will be "light" (^{14}N-^{14}N), as the ^{14}N strand from the hybrid replicates with new ^{14}N.
    - Half of the molecules will remain "intermediate" (^{15}N-^{14}N), as the ^{15}N strand from the hybrid replicates with new ^{14}N.
- **Observation:** When DNA is extracted from these cells and centrifuged, it will form **two distinct bands**:

- One band at the **intermediate density** position.
- Another band at the **light density** position (top of the tube).
- The intensity of the light band will be equal to the intensity of the intermediate band.

- **Conclusion:**
  - The results perfectly matched the predictions of the semi-conservative model.
  - The appearance of a single intermediate band after one generation ruled out the conservative model (which would predict separate heavy and light bands).
  - The appearance of two bands (intermediate and light) after the second generation, with equal intensity, ruled out the dispersive model (which would predict a single, progressively lighter band).

Duhive

This experiment provided conclusive evidence that DNA replication proceeds via a semi-conservative mechanism, ensuring that genetic information is faithfully transmitted.

4. **(a) With the help of suitable diagram describe the process of transcription in Eukaryotes. (10)**

The user requested not to make diagrams or structures. Therefore, a detailed description of eukaryotic transcription will be provided without a diagram.

Process of Transcription in Eukaryotes:

Transcription is the process by which genetic information encoded in DNA is copied into an RNA molecule. In eukaryotes, this process is significantly more complex than in prokaryotes due to several factors: larger and linear genomes, chromatin structure, presence of introns, and multiple RNA polymerases. Eukaryotic transcription occurs in the nucleus, with subsequent processing and transport of RNA to the cytoplasm.

There are three main types of RNA polymerases (RNAPs) in eukaryotes, each responsible for transcribing different classes of genes:

- **RNA Polymerase I (RNAP I):** Synthesizes most ribosomal RNAs (rRNAs), specifically 28S, 18S, and 5.8S rRNA.
- **RNA Polymerase II (RNAP II):** Synthesizes messenger RNAs (mRNAs) encoding proteins, and some small RNAs (e.g., snRNAs, snoRNAs, miRNAs). This is the most studied and complex one.
- **RNA Polymerase III (RNAP III):** Synthesizes transfer RNAs (tRNAs), 5S rRNA, and other small RNAs (e.g., U6 snRNA).

The general process of transcription for protein-coding genes (catalyzed by RNAP II) can be divided into three stages: initiation, elongation, and termination.

1. Initiation:

Duhive

- **Promoter Recognition:** Eukaryotic promoters are more complex than prokaryotic ones. For RNAP II, common promoter elements include:
    - **TATA box:** A consensus sequence (TATAAA) located about 25-30 base pairs upstream of the transcription start site (+1). It is recognized by the TATA-binding protein (TBP).
    - **Initiator element (Inr):** A sequence encompassing the transcription start site.
    - **Downstream promoter elements (DPE):** Found downstream of the start site in some TATA-less promoters.
    - **Enhancers:** Regulatory DNA sequences located far from the promoter (up to thousands of base pairs away, either upstream or downstream, or within introns). They bind to specific activator proteins that interact with the transcription machinery to enhance transcription.
- **Assembly of Pre-initiation Complex (PIC):**

- Unlike prokaryotic RNA polymerase, eukaryotic RNAPs cannot directly bind to the promoter. They require a large set of accessory proteins called **general transcription factors (GTFs)**.
- The GTFs (TFIIA, TFIIB, TFIID, TFIIE, TFIIF, TFIIH) assemble sequentially at the promoter to form the PIC.
- **TFIID**, which contains TBP, is usually the first GTF to bind to the TATA box (or other core promoter elements).
- The binding of TFIID facilitates the recruitment of other GTFs and RNAP II to the promoter, forming a stable complex.

- **RNAP II Phosphorylation and Promoter Clearance:**
  - **TFIIH**, a GTF with helicase activity, unwinds the DNA around the transcription start site, creating an open complex.
  - TFIIH also has kinase activity, which phosphorylates the C-terminal domain (CTD) of the largest subunit of RNAP II.
  - This phosphorylation is a key event that signals the transition from initiation to elongation, allowing RNAP II to dissociate from most GTFs and move along the DNA template.

Duhive

2. Elongation:

- **RNA Synthesis:** RNAP II moves along the DNA template strand in the 3' to 5' direction, synthesizing the RNA molecule in the 5' to 3' direction.
- **Nucleotide Addition:** It adds ribonucleoside triphosphates (ATP, UTP, CTP, GTP) one by one, forming phosphodiester bonds, using the complementary base pairing rules (A with U, T with A, G with C, C with G).
- **Processivity:** The elongation phase is highly processive, meaning RNAP II can synthesize long stretches of RNA without dissociating from the DNA template.

- **Elongation Factors:** Various elongation factors associate with RNAP II during this phase to enhance its processivity, suppress pausing, and coordinate with RNA processing events.
- **Chromatin Remodeling:** As RNAP II moves, nucleosomes ahead of the polymerase are transiently disassembled or modified, and then reassembled behind it, ensuring access to the DNA template.

3. Termination:

- **Lack of Specific Terminator Sequences:** Unlike prokaryotes, eukaryotes do not have clearly defined terminator sequences like Rho-dependent or Rho-independent terminators.
- **Polyadenylation Signal:** For protein-coding genes (mRNAs), termination is often linked to the processing of the 3' end of the RNA. The primary transcript contains a **polyadenylation signal sequence** (e.g., AAUAAA) downstream of the coding region.
- **Cleavage and Polyadenylation:**
    - After RNAP II transcribes past the polyadenylation signal, specific protein complexes (including **CPSF - Cleavage and Polyadenylation Specificity Factor** and CstF - Cleavage Stimulation Factor) recognize and bind to this sequence.
    - The RNA molecule is then cleaved downstream of the polyadenylation signal.
    - Subsequently, **poly(A) polymerase (PAP)** adds a string of adenosine nucleotides (a poly-A tail, typically 50-250 As) to the 3' end of the newly cleaved RNA. This poly-A tail is important for mRNA stability, transport to the cytoplasm, and translation efficiency.
- **RNAP II Dissociation:** The addition of the poly-A tail and the subsequent processing events are thought to trigger the dissociation of RNAP II from the DNA template, although the exact mechanism is still under investigation. Some models suggest that phosphorylation patterns on the CTD of RNAP II

Duhive

or specialized termination factors may also play a role. The unprocessed RNA downstream of the cleavage site is often degraded.

This intricate process of eukaryotic transcription ensures tight control over gene expression, allowing for the precise regulation necessary for complex multicellular organisms.

(b) Write down the main differences between eukaryotic and prokaryotic translation. (5)

Translation is the process of synthesizing proteins from an mRNA template. While the fundamental principles are conserved, there are several key differences between eukaryotic and prokaryotic translation, reflecting their distinct cellular organization and regulatory complexities.

- **1. Location:**
    - **Prokaryotes:** Translation is coupled with transcription. Ribosomes often attach to the mRNA and begin protein synthesis even before the mRNA transcript is fully synthesized. Both processes occur in the cytoplasm.
    - **Eukaryotes:** Transcription occurs in the nucleus, and the resulting mRNA must be processed (splicing, capping, polyadenylation) and then exported to the cytoplasm where translation takes place on ribosomes. They are spatially and temporally separated.
- **2. Ribosome Size and Composition:**
    - **Prokaryotes:** Have smaller 70S ribosomes, composed of a 30S small subunit and a 50S large subunit.
    - **Eukaryotes:** Have larger 80S ribosomes, composed of a 40S small subunit and a 60S large subunit.
- **3. mRNA Structure and Processing:**
    - **Prokaryotes:** mRNA is typically polycistronic (can encode multiple proteins from a single mRNA molecule, each with its own start and stop codon). It lacks a 5' cap and a poly-A tail.

Duhive

  - **Eukaryotes:** mRNA is generally monocistronic (encodes only one protein). It undergoes significant processing: a 5' cap (7-methylguanosine) is added, introns are spliced out, and a poly-A tail is added to the 3' end. These modifications are crucial for stability, transport, and translation initiation.

- **4. Initiation of Translation:**
  - **Prokaryotes:** Ribosomes bind to a specific **Shine-Dalgarno sequence** (ribosome-binding site) located a few nucleotides upstream of the start codon (AUG). This sequence pairs with a complementary sequence on the 16S rRNA of the small ribosomal subunit, correctly positioning the ribosome.
  - **Eukaryotes:** Ribosomes bind to the 5' cap of the mRNA and then scan downstream in the 5' to 3' direction until they encounter the first AUG codon, which is typically the start codon (Kozak sequence often surrounds it for optimal initiation). This is known as the **scanning mechanism**.

Duhive

- **5. Initiator tRNA and Amino Acid:**
  - **Prokaryotes:** The initiator tRNA carries N-formylmethionine (fMet).
  - **Eukaryotes:** The initiator tRNA carries unmodified methionine (Met).
- **6. Initiation Factors:**
  - **Prokaryotes:** Require three initiation factors (IF-1, IF-2, IF-3).
  - **Eukaryotes:** Require a larger and more complex set of initiation factors (eIFs), including eIF4E (binds to 5' cap), eIF4G (scaffolding protein), and eIF2 (involved in Met-tRNAi loading).
- **7. Termination Factors:**
  - **Prokaryotes:** Have three release factors (RF1, RF2, RF3).

- **Eukaryotes:** Have a single eukaryotic release factor (eRF1) for all three stop codons, and eRF3.

- **8. Polysomes (Polyribosomes):**
  - **Prokaryotes:** Since transcription and translation are coupled, ribosomes can attach to mRNA even before transcription is complete, forming **polysomes** (multiple ribosomes translating the same mRNA simultaneously), which appear as beads on a string.
  - **Eukaryotes:** Polysomes also form, but they occur in the cytoplasm on mature mRNA molecules after export from the nucleus.

These differences highlight the increasing complexity and regulatory control over gene expression in eukaryotes compared to the more streamlined and coupled processes in prokaryotes.

5. **(a) What is cell signalling and importance of second messengers? Write the major differences of hormone signalling mechanism of nuclear receptor pathway and cell surface receptor pathway? (10)**

Duhive

What is Cell Signalling?

Cell signalling (or cell communication) is the complex system by which cells communicate with each other and respond to their environment. It involves the transmission of information from outside the cell to inside, leading to a specific cellular response. This process is fundamental for all aspects of life, including growth, development, metabolism, tissue repair, and immune responses.

The general steps in cell signalling include:

10. **Signal Reception:** A signaling molecule (ligand, e.g., hormone, neurotransmitter, growth factor) binds to a specific receptor protein on or within the target cell.
11. **Signal Transduction:** The binding of the ligand to the receptor triggers a series of biochemical events inside the cell, often involving a cascade of molecular interactions. This converts the extracellular signal into an intracellular response.

12. **Cellular Response:** The transduced signal leads to a specific cellular activity, such as changes in gene expression, enzyme activity, cell division, secretion, or cell movement.
13. **Signal Termination:** The signal is eventually terminated to ensure that the cell can respond to new signals and maintain proper homeostasis.

Importance of Second Messengers:

Second messengers are small, non-protein, intracellular signaling molecules that relay signals from receptors on the cell surface to target molecules within the cytoplasm or nucleus. They act as amplifying agents and diffusers of the initial signal.

- **Amplification:** A single ligand binding to a receptor can lead to the production of many second messenger molecules, each of which can activate multiple downstream targets. This amplifies the initial signal, allowing a small extracellular stimulus to elicit a large and rapid cellular response.
- **Diffusion:** Being small and diffusible, second messengers can quickly spread the signal throughout the cell, reaching various intracellular targets distant from the receptor.
- **Diverse Responses:** Different second messengers can activate distinct downstream pathways, leading to a variety of cellular responses, even from the same initial signal or receptor type.
- **Integration:** Multiple signaling pathways can converge on the same second messenger, allowing cells to integrate different extracellular signals and produce a coordinated response.
- **Speed:** Their small size allows for rapid generation and diffusion, enabling quick cellular responses.
- **Modulation:** The concentration of second messengers can be tightly regulated by specific enzymes, allowing for precise control and termination of the signal.

Examples of Common Second Messengers:

Duhive

- **cAMP (cyclic AMP):** Involved in adrenaline signaling, glycogen breakdown.
- **cGMP (cyclic GMP):** Involved in smooth muscle relaxation, vision.
- **Ca^{2+} (calcium ions):** Involved in muscle contraction, neurotransmitter release, enzyme activation.
- **IP_3 (inositol 1,4,5-trisphosphate) and DAG (diacylglycerol):** Involved in release of intracellular calcium and activation of protein kinase C.

Major Differences in Hormone Signalling Mechanism: Nuclear Receptor Pathway vs. Cell Surface Receptor Pathway

The mechanism of hormone signaling largely depends on the chemical nature of the hormone and its ability to cross the plasma membrane. This leads to two major pathways: those involving nuclear receptors (for lipid-soluble hormones) and those involving cell surface receptors (for water-soluble hormones).

Duhive

- **1. Nature of Ligand (Hormone):**
    - **Nuclear Receptor Pathway:** Ligands are typically **lipid-soluble hormones** (e.g., steroid hormones like estrogen, testosterone, cortisol; thyroid hormones; retinoids; vitamin D). They can readily pass through the hydrophobic plasma membrane.
    - **Cell Surface Receptor Pathway:** Ligands are typically **water-soluble hormones** (e.g., peptide hormones like insulin, growth hormone; catecholamines like adrenaline; neurotransmitters). They cannot easily cross the plasma membrane.
- **2. Location of Receptor:**
    - **Nuclear Receptor Pathway:** Receptors are located **inside the cell**, either in the cytoplasm or directly within the nucleus.
    - **Cell Surface Receptor Pathway:** Receptors are **transmembrane proteins** embedded in the plasma membrane, with their ligand-binding domain facing the extracellular space.

- **3. Signal Transduction Mechanism:**
    - **Nuclear Receptor Pathway:**
        - The hormone directly diffuses across the plasma membrane and binds to its specific nuclear receptor.
        - Upon ligand binding, the receptor undergoes a conformational change, often dissociating from chaperone proteins.
        - The hormone-receptor complex then translocates to the nucleus (if it was initially in the cytoplasm) and binds directly to specific DNA sequences called **Hormone Response Elements (HREs)** in the promoter or enhancer regions of target genes.
        - The activated complex acts as a **transcription factor**, directly modulating gene expression (either activating or repressing transcription).
        - **No second messengers** are typically involved in the direct signaling from receptor to DNA.
    - **Cell Surface Receptor Pathway:**
        - The hormone binds to the extracellular domain of its cell surface receptor.
        - This binding causes a conformational change in the receptor, which then transduces the signal across the membrane to the intracellular side.
        - This often involves a cascade of events, including the activation of G proteins, receptor tyrosine kinases (RTKs), or ion channels.
        - Crucially, **second messengers** (e.g., cAMP, Ca^{2+}, IP_3, DAG) are frequently generated or released inside the cell to amplify and relay the signal to various intracellular targets.

Duhive

    - The final response often involves changes in enzyme activity, protein phosphorylation, or indirectly, changes in gene expression through transcription factor activation.

- **4. Speed and Duration of Response:**
    - **Nuclear Receptor Pathway:** Responses are generally **slower** (minutes to hours) because they involve changes in gene expression (transcription and subsequent protein synthesis). However, the effects can be **long-lasting**.
    - **Cell Surface Receptor Pathway:** Responses are typically **rapid** (seconds to minutes) because they often involve activation of existing enzymes or channels. The effects are usually **transient** unless the signal is continuously present.
- **5. Examples:**
    - **Nuclear Receptor Pathway:** Regulation of metabolism by cortisol, sexual development by estrogen/testosterone, calcium homeostasis by vitamin D.
    - **Cell Surface Receptor Pathway:** Glucose uptake by insulin, fight-or-flight response by adrenaline, neurotransmission.

Duhive

In summary, the choice of signaling pathway depends on the hormone's ability to traverse the cell membrane, dictating whether the receptor is intracellular or on the surface, and consequently, whether the signal is transduced directly to the nucleus or relies on an intricate network of second messengers for intracellular propagation.

6. **(b) What is end replication problem? Discuss the role of telomerase in replication of 5' end of linear chromosome. (5)**

The question asks about 6(b) and then lists short notes (a) to (d). I will answer 6(b) directly and then select three from the short notes as requested.

6. (b) What is end replication problem? Discuss the role of telomerase in replication of 5' end of linear chromosome. (5)

What is the End Replication Problem?

The end-replication problem refers to the inability of conventional DNA polymerases to fully replicate the very ends of linear eukaryotic chromosomes. This leads to a progressive shortening of the chromosome ends with each round of DNA replication.

- **Mechanism of the Problem:**
    - DNA replication proceeds bidirectionally from origins of replication.
    - The **leading strand** is synthesized continuously towards the replication fork.
    - The **lagging strand** is synthesized discontinuously in Okazaki fragments. Each Okazaki fragment requires an RNA primer.
    - When the replication fork reaches the end of a linear chromosome, the leading strand can be completely synthesized up to the very end of its template.
    - However, for the lagging strand, once the final RNA primer is removed from the 5' end of the newly synthesized strand, there is no upstream 3'-OH group available for DNA polymerase to fill the resulting gap.
    - This means that a small portion of the template strand at the very 3' end cannot be replicated. Consequently, with each round of replication, the new DNA molecule becomes slightly shorter than the parental molecule, specifically at its 5' end.

Duhive

Role of Telomerase in Replication of 5' end of Linear Chromosome:

Telomeres are specialized repetitive DNA sequences (e.g., TTAGGG in humans) found at the ends of eukaryotic linear chromosomes. They protect the ends of chromosomes from degradation and fusion, and they are maintained by an enzyme called **telomerase**. Telomerase solves the end-replication problem by extending the 3' end of the parental DNA strand, thereby providing a template for the lagging strand synthesis machinery.

- **Telomerase Structure:** Telomerase is a unique reverse transcriptase enzyme. It is a ribonucleoprotein, meaning it consists of both protein and an RNA component:
    - **TERT (Telomerase Reverse Transcriptase):** The protein component with reverse transcriptase activity.
    - **TERC (Telomerase RNA Component):** An integral RNA molecule that contains a template sequence complementary to the telomeric DNA repeat (e.g., 3'-AAUCCC-5' in humans).
- **Mechanism of Action (Extending the 3' end):**
    a. **Binding:** Telomerase binds to the 3' overhang (the longer, single-stranded 3' end) of the parental DNA strand at the telomere. The TERC RNA component base-pairs with the existing telomeric DNA sequence.
    b. **Reverse Transcription:** Using its internal TERC RNA as a template, the TERT protein (reverse transcriptase activity) synthesizes new DNA (deoxyribonucleotides) that extends the 3' end of the parental DNA strand. It essentially adds multiple copies of the telomeric repeat sequence.
    c. **Translocation and Repeat:** After synthesizing a few repeats, telomerase translocates (moves along) to the newly synthesized end and repeats the process, adding more telomeric repeats. This process effectively extends the 3' overhang.
    d. **Lagging Strand Synthesis:** Once the 3' end of the parental strand has been sufficiently extended by telomerase, a conventional RNA primer can be synthesized by primase on this extended template.
    e. **DNA Polymerase Action:** DNA polymerase can then extend this primer to fill in the gap on the newly synthesized lagging strand.
    f. **Primer Removal:** The RNA primer is eventually removed, leaving a small gap, but critically, the overall length of the telomere is

Duhive

maintained, preventing the loss of genetic information from the main chromosome.

Significance: Telomerase activity is essential for maintaining telomere length in germ cells, embryonic stem cells, and frequently dividing cells like hematopoietic stem cells, ensuring genome stability across generations. In most somatic cells, telomerase activity is very low or absent, leading to telomere shortening with each division, which acts as a "mitotic clock" contributing to cellular senescence (aging) and eventually apoptosis. Conversely, many cancer cells reactivate telomerase, allowing them to proliferate indefinitely.

Short Notes (Any Three): (3×5=15)

- **(a) Alternative splicing**
    - **Definition:** Alternative splicing is a regulated molecular process that allows a single gene to encode multiple different protein isoforms (variants) by selectively including or excluding various exons from the primary RNA transcript (pre-mRNA). It is a crucial mechanism for generating protein diversity and regulating gene expression in eukaryotes.
    - **Mechanism:** In eukaryotic genes, coding regions (exons) are interrupted by non-coding regions (introns). After transcription, the entire gene is transcribed into a pre-mRNA. During splicing, spliceosomes (complexes of snRNAs and proteins) remove introns and ligate exons together. In alternative splicing, this process is regulated such that different combinations of exons are joined, producing distinct mature mRNA molecules from the same pre-mRNA.
    - **Types of Alternative Splicing:** Common patterns include:
        - **Exon skipping:** An exon is completely excluded from the mature mRNA.
        - **Mutually exclusive exons:** One of two exons is retained, but never both.

Duhive

        - **Alternative 5' or 3' splice sites:** Different splice sites within an intron or exon are used, leading to longer or shorter exons.
        - **Intron retention:** An intron is retained in the mature mRNA, which can lead to a truncated protein or nonsense-mediated decay.
    - **Regulation:** Alternative splicing is tightly regulated by specific RNA-binding proteins called splicing activators and splicing repressors, which bind to regulatory sequences (enhancers and silencers) within the pre-mRNA. These proteins can either promote or inhibit the recognition of specific splice sites.
    - **Significance:**
        - **Protein Diversity:** Greatly expands the coding capacity of the genome. For example, the human genome has ~20,000 protein-coding genes, but produces hundreds of thousands of distinct proteins largely due to alternative splicing.
        - **Cell-Type Specificity:** Allows different cell types or tissues to express different protein isoforms from the same gene, contributing to specialized functions.
        - **Development and Disease:** Crucial for normal development, and dysregulation of alternative splicing is implicated in various diseases, including cancer, neurological disorders, and genetic diseases.

Duhive

- **(b) Lac Operon**
    - **Definition:** The *lac* operon is a classic example of an inducible operon in *Escherichia coli* and other bacteria, responsible for the metabolism of lactose. An operon is a cluster of genes under the control of a single promoter and operator, allowing for coordinated gene expression. The *lac* operon is typically "off" and is turned "on" in the presence of lactose.
    - **Components:** The *lac* operon consists of:

- **Structural Genes:**
    - *lacZ*: Encodes β-galactosidase, which breaks down lactose into glucose and galactose.
    - *lacY*: Encodes lactose permease, a protein that transports lactose into the bacterial cell.
    - *lacA*: Encodes transacetylase, whose precise role in lactose metabolism is less clear but may be involved in detoxification.
- **Promoter (P):** The DNA sequence where RNA polymerase binds to initiate transcription.
- **Operator (O):** A DNA sequence located between the promoter and the structural genes, where the repressor protein binds.
- **Regulatory Gene (*lacI*):** Located upstream of the operon, it encodes the *lac* repressor protein.

Duhive

- **Regulation:** The *lac* operon is under dual control:
    - **Negative Regulation (by *lac* Repressor):**
        - In the **absence of lactose**, the *lac* repressor protein (encoded by *lacI*) is constitutively expressed and binds tightly to the operator (O) sequence.
        - This binding physically blocks RNA polymerase from binding to the promoter or initiating transcription of the structural genes. Thus, lactose-metabolizing enzymes are not produced.
        - In the **presence of lactose**, lactose (or its isomer, allolactose, which is the actual inducer) binds to the *lac* repressor. This binding causes a conformational change in the repressor, reducing its affinity for the operator. The

repressor detaches from the operator, allowing RNA polymerase to transcribe the structural genes.

- **Positive Regulation (by CAP-cAMP):**
    - This mechanism ensures that the *lac* operon is strongly expressed only when glucose (the preferred energy source) is absent.
    - When **glucose levels are low**, cyclic AMP (cAMP) levels are high. cAMP binds to the **Catabolite Activator Protein (CAP)**, forming the CAP-cAMP complex.
    - The CAP-cAMP complex binds to a specific site near the *lac* promoter. This binding enhances the affinity of RNA polymerase for the promoter, stimulating transcription significantly.
    - When **glucose levels are high**, cAMP levels are low, so CAP-cAMP complex does not form. Even if lactose is present, transcription of the *lac* operon will be minimal (basal level) because CAP is not bound to activate it. This phenomenon is called **catabolite repression**.

Duhive

- **Conclusion:** The *lac* operon's regulation ensures that bacteria only produce enzymes for lactose metabolism when lactose is available and, more importantly, when glucose is scarce, demonstrating an economical and efficient use of resources.

- **(c) Synthesis of rRNA**
    - **Definition:** Ribosomal RNAs (rRNAs) are structural and catalytic components of ribosomes, the cellular machinery responsible for protein synthesis. Their synthesis is a highly regulated and essential process, occurring primarily in the nucleolus in eukaryotes and in the cytoplasm in prokaryotes.
    - **In Eukaryotes:**

- **RNA Polymerase I (RNAP I):** Most rRNA genes (18S, 5.8S, and 28S rRNAs) are transcribed as a single large precursor molecule (45S pre-rRNA) by RNA Polymerase I in the nucleolus. The 5S rRNA is transcribed by RNA Polymerase III outside the nucleolus.
- **Nucleolar Location:** The nucleolus is a distinct sub-nuclear structure dedicated to rRNA synthesis, processing, and ribosome assembly. It is rich in rRNA genes, RNAP I, and associated proteins.
- **Processing of Pre-rRNA:** The 45S pre-rRNA undergoes extensive chemical modifications (e.g., methylation of bases and ribose sugars) and precise cleavage events by small nucleolar RNAs (snoRNAs) and various nucleases. These modifications are crucial for proper folding and function of mature rRNAs.
- **Ribosome Assembly:** As the rRNAs are being processed, they associate with ribosomal proteins (which are synthesized in the cytoplasm and imported into the nucleolus). This self-assembly process leads to the formation of the large (60S, containing 28S, 5.8S, 5S rRNAs) and small (40S, containing 18S rRNA) ribosomal subunits.
- **Export:** The mature ribosomal subunits are then exported from the nucleolus to the cytoplasm through nuclear pores, where they assemble into functional 80S ribosomes for translation.

Duhive

- **In Prokaryotes:**
  - **Single Operon:** Prokaryotic rRNAs (16S, 23S, and 5S) are typically encoded within a single operon and are transcribed as a single large precursor RNA by a single **RNA polymerase**.
  - **Processing:** The precursor rRNA is subsequently processed by specific ribonucleases (RNases) to yield the mature 16S, 23S, and 5S rRNAs.

        - **Coupled Assembly:** Ribosomal proteins bind to the nascent rRNA during or immediately after transcription, leading to the assembly of 30S and 50S ribosomal subunits in the cytoplasm. These combine to form 70S ribosomes.
        - **No Nucleolus:** Prokaryotic cells lack a nucleolus; all steps occur in the cytoplasm.
    - **Significance:** rRNA synthesis is a highly energy-intensive process that accounts for a large fraction of a cell's transcriptional activity. The accurate and efficient production of rRNAs is vital for protein synthesis and, consequently, for cell growth and survival.

- **(d) RNA editing**
    - **Definition:** RNA editing is a post-transcriptional modification process that alters the nucleotide sequence of an RNA molecule after it has been transcribed from DNA. This alteration can involve the insertion, deletion, or substitution of nucleotides, leading to a mature RNA sequence that differs from its genomic template.
    - **Types of RNA Editing:**
        - **Substitution Editing:** The most common type, involving the chemical alteration of one base to another.
            - **C to U editing:** Cytosine is deaminated to uracil (C → U). A prominent example is the APOB gene in humans; in the liver, unedited APOB mRNA produces ApoB-100 (a full-length protein), while in the intestine, C-to-U editing at a specific site creates a premature stop codon, leading to the synthesis of a shorter ApoB-48 protein.
            - **A to I editing:** Adenosine is deaminated to inosine (A → I). Inosine is read as guanosine (G) by the ribosome. This type of editing is widespread in the nervous system and affects many genes, often altering protein sequence or

Duhive

splice sites. It is catalyzed by adenosine deaminases acting on RNA (ADARs).

- **Insertion/Deletion Editing:** Involves the addition or removal of nucleotides from the RNA sequence. This is particularly prevalent in the mitochondria of trypanosomes (a group of protozoan parasites), where guide RNAs (gRNAs) direct the insertion or deletion of specific uridines.

- **Mechanism:** RNA editing is enzyme-catalyzed. For C-to-U editing, specific deaminases are involved. For A-to-I editing, ADAR enzymes are responsible, often acting on double-stranded RNA structures formed by base-pairing within the transcript. Insertion/deletion editing in trypanosomes involves complex multi-protein machinery.

- **Significance:**

  - **Increased Protein Diversity:** Allows a single gene to encode multiple functionally distinct proteins, similar to alternative splicing.

  - **Regulation of Gene Expression:** Can alter splice sites, create or remove start/stop codons, or change amino acid sequences, thereby impacting protein function, stability, or localization.

  - **Evolutionary Adaptation:** May contribute to adaptation and phenotypic plasticity in response to environmental changes.

  - **Disease Relevance:** Dysregulation of RNA editing is linked to various human diseases, including neurological disorders (e.g., ALS, epilepsy) and cancer.

- **Distinction from DNA Mutation:** RNA editing is a post-transcriptional process and does not alter the underlying DNA sequence. Therefore, it is not inheritable in the same way as DNA mutations.

Duhive