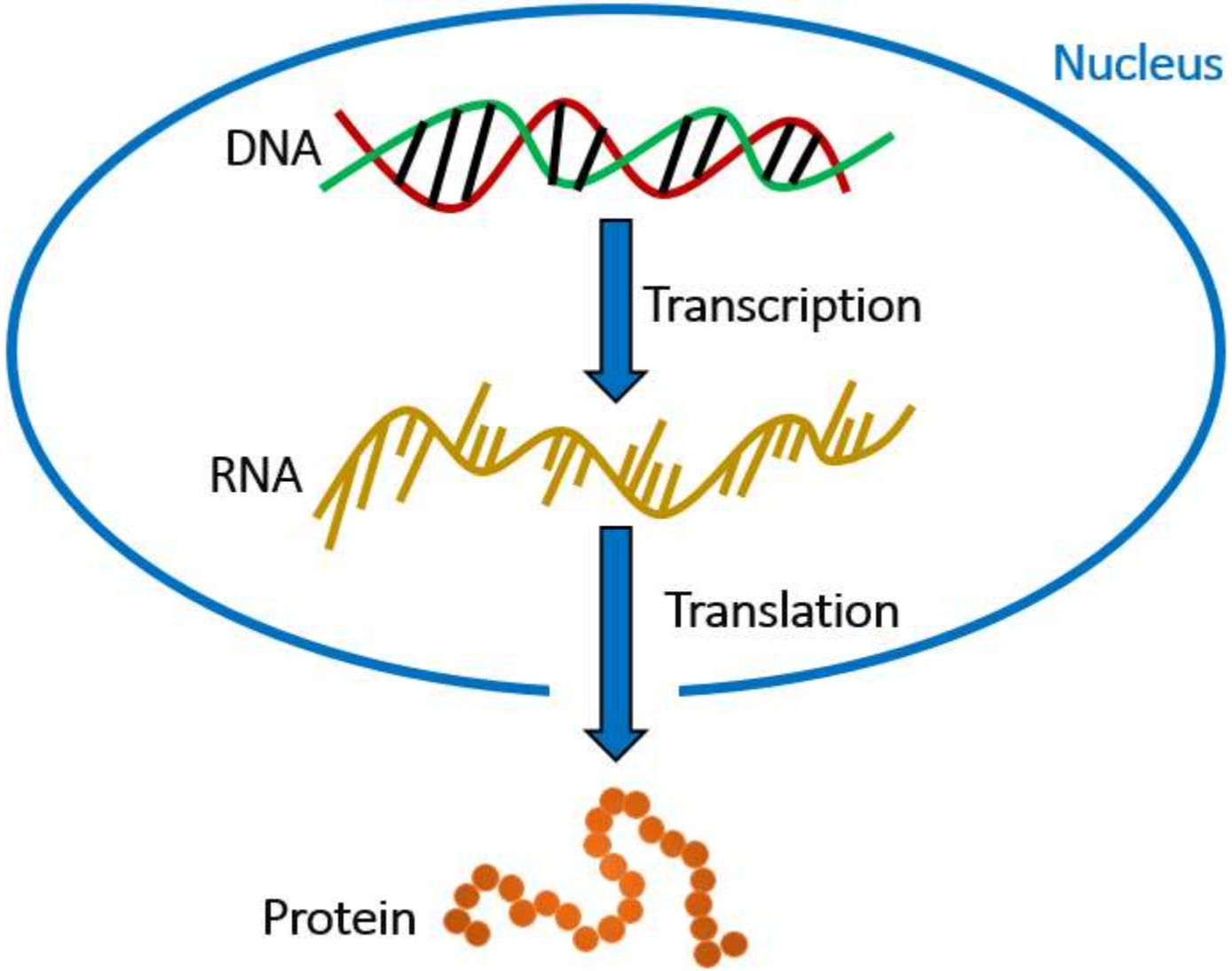
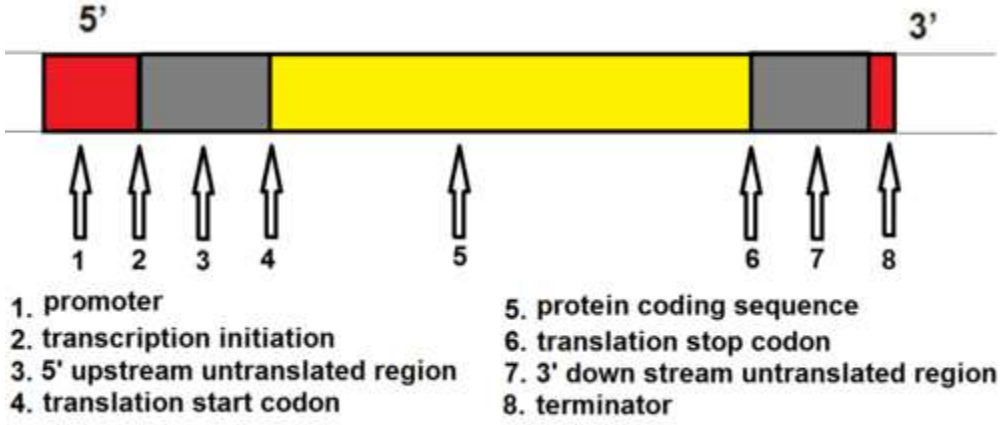
# Protein synthesis

**Central dogma**

DNA → RNA → Protein



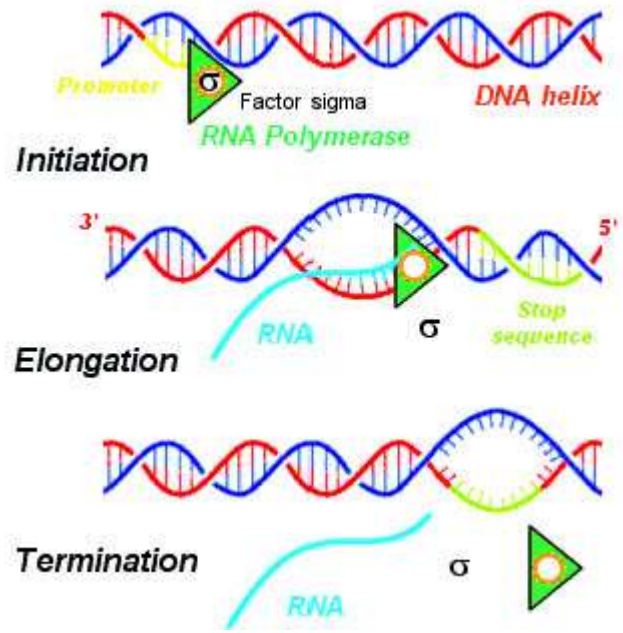
# Steps in protein synthesis




- The two processes involved in the central dogma are **transcription** and **translation.**
- **Transcription** is the first part of the central dogma of molecular biology: **DNA → RNA**. It is the transfer of genetic instructions in DNA to mRNA. Transcription happens in the nucleus of the cell.
- During transcription, a strand of mRNA is made that is complementary to a strand of DNA called gene. A gene can easily be identified from the DNA sequence. A gene contains the basic three regions, promoter, coding sequence, and terminator.

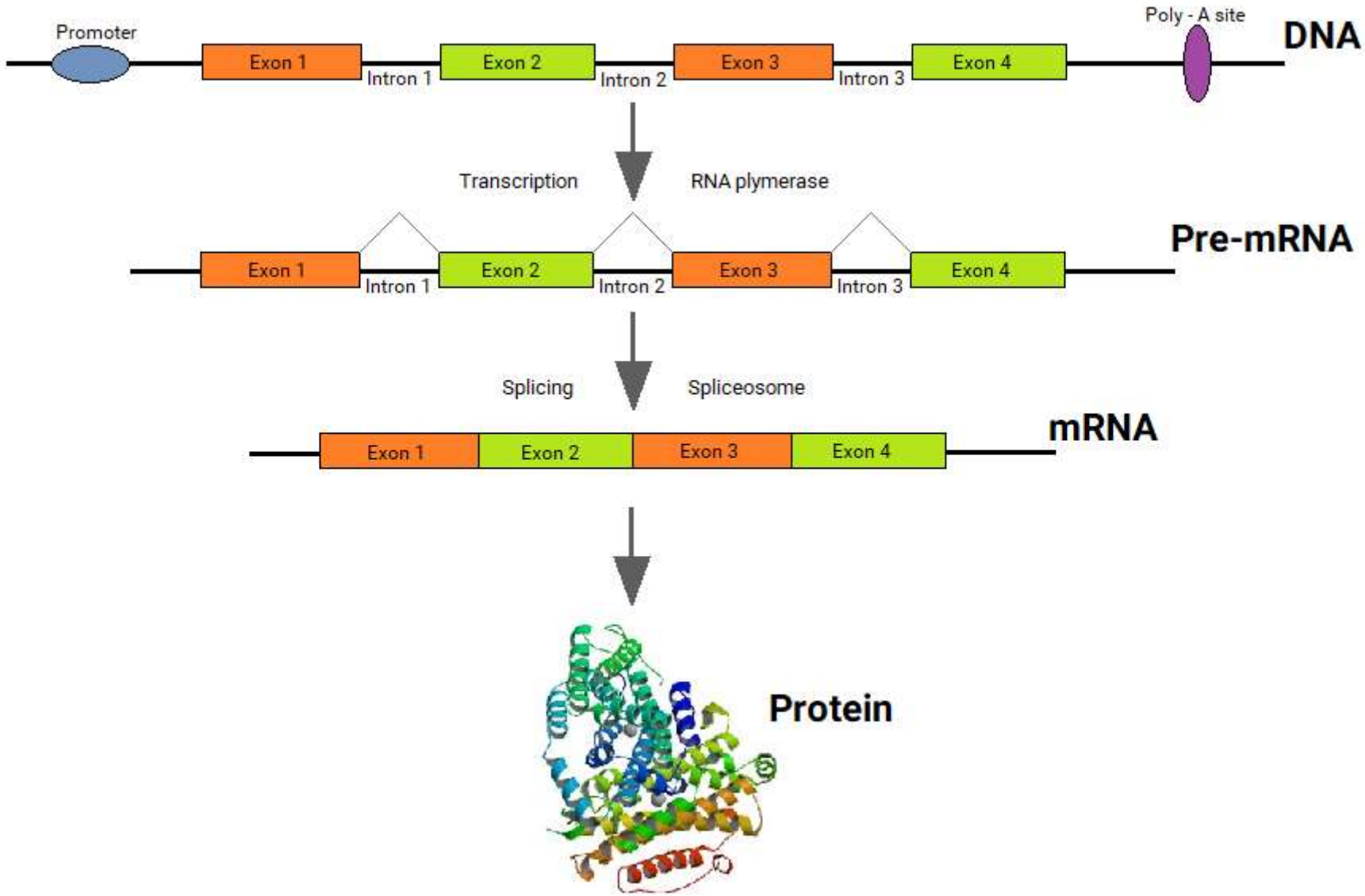
# Steps of Transcription

- Transcription takes place in three steps, called initiation, elongation, and termination. The steps are illustrated in the figure below.
- Initiation is the beginning of transcription. It occurs when the enzyme RNA polymerase binds to a region of a gene called the **promoter**. This signals the DNA to unwind so the enzyme can "read" the bases in one of the DNA strands. The enzyme is ready to make a strand of mRNA with a complementary sequence of bases. The promoter is not part of the resulting mRNA
- Elongation is the addition of nucleotides to the mRNA strand.
- Termination is the ending of transcription. As RNA polymerase transcribes terminator, it detaches from DNA. The mRNA strand is complete after this step.



# Processing mRNA

- In eukaryotes, the new mRNA is not yet ready for translation. At this stage, it is called pre-mRNA, and it must go through more processing before it leaves the nucleus as mature mRNA. The processing may include addition of a 5' cap, splicing, editing, and 3' polyadenylation tail. These processes modify the mRNA in various ways. Such modifications allow a single gene to be used to make more than one protein.
- 5' cap protects mRNA in the cytoplasm and helps in attachment of mRNA with ribosome for translation.
- Splicing removes introns from the protein coding sequence of mRNA, as shown in the diagram below. **Introns** are regions that do not code for the protein. The remaining mRNA consists only of regions called **exons** that do code for the protein. The ribonucleoproteins in the diagram are small proteins in the nucleus that contain RNA and are needed for the splicing process.
- Editing changes some of the nucleotides in mRNA. For example, a human protein called APOB, which helps transport lipids in the blood, has two different forms because of editing. One form is smaller than the other because editing adds an earlier stop signal in mRNA.
- Polyadenylation adds a “tail” to the mRNA. The tail consists of a string of As (adenine bases). It signals the end of mRNA. It is also involved in exporting mRNA from the nucleus, and it protects mRNA from enzymes that might break it down.


Promoter
Exon 1
Intron 1
Exon 2
Intron 2
Exon 3
Intron 3
Exon 4
Poly - A site
DNA
Transcription
RNA plymerase
Pre-mRNA
Splicing
Spliceosome
mRNA
Protein

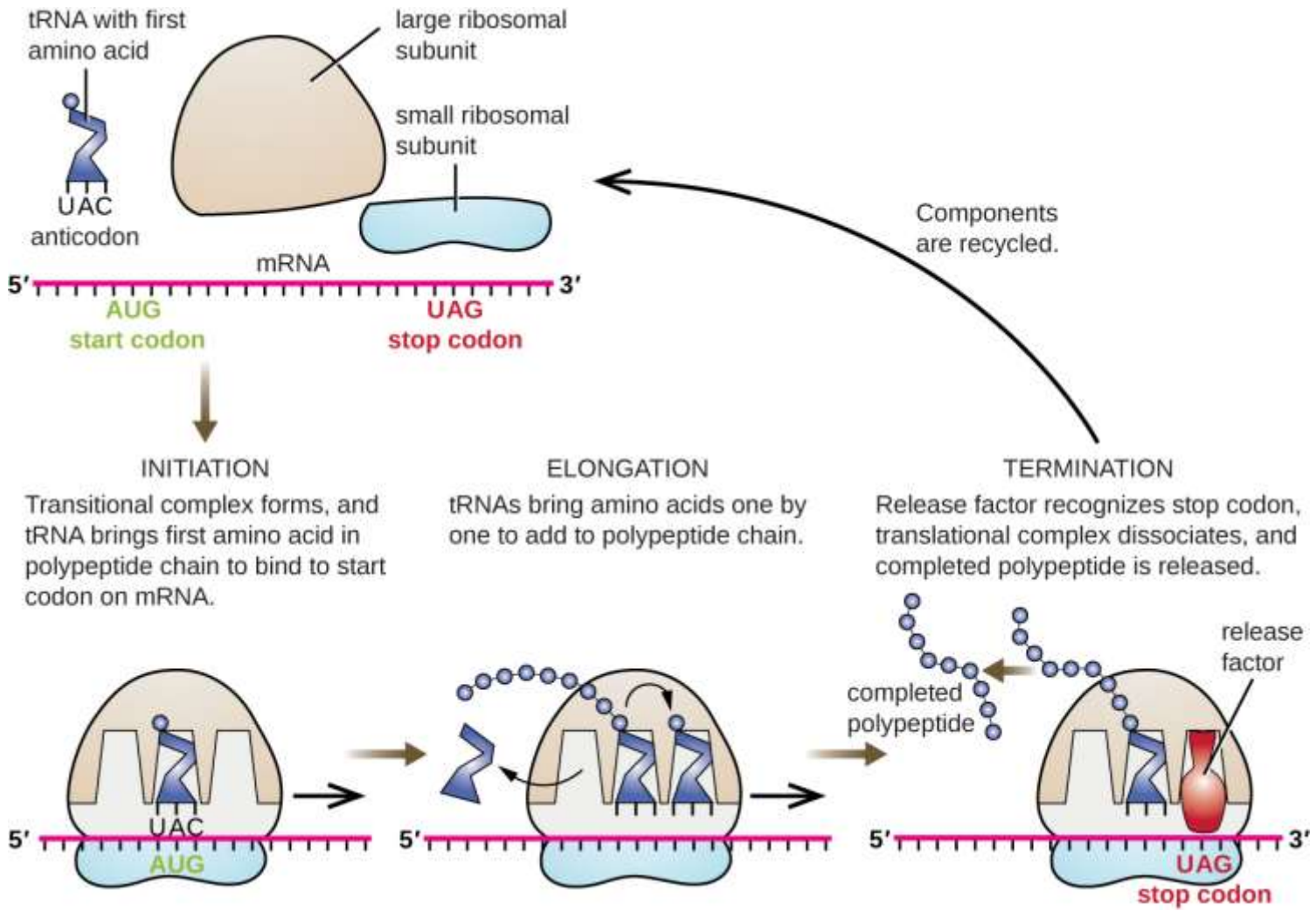
# Translation

- **The translation** is the second part of the central dogma of molecular biology: **RNA --> Protein**.
- It is the process in which the genetic code in mRNA is read to make a protein. After mRNA leaves the nucleus, it moves to a ribosome, which consists of rRNA and proteins.
- Translation happens on the ribosomes floating in the cytosol, or on the ribosomes attached to the rough endoplasmic reticulum.
- The ribosome reads the sequence of codons in mRNA, and molecules of tRNA bring amino acids to the ribosome in the correct sequence.
- Just as with mRNA synthesis, protein synthesis can be divided into three phases: initiation, elongation, and termination.
- In addition to the mRNA template and ribosomes, many other molecules contribute to the process of translation, such as tRNAs and various enzymatic factors

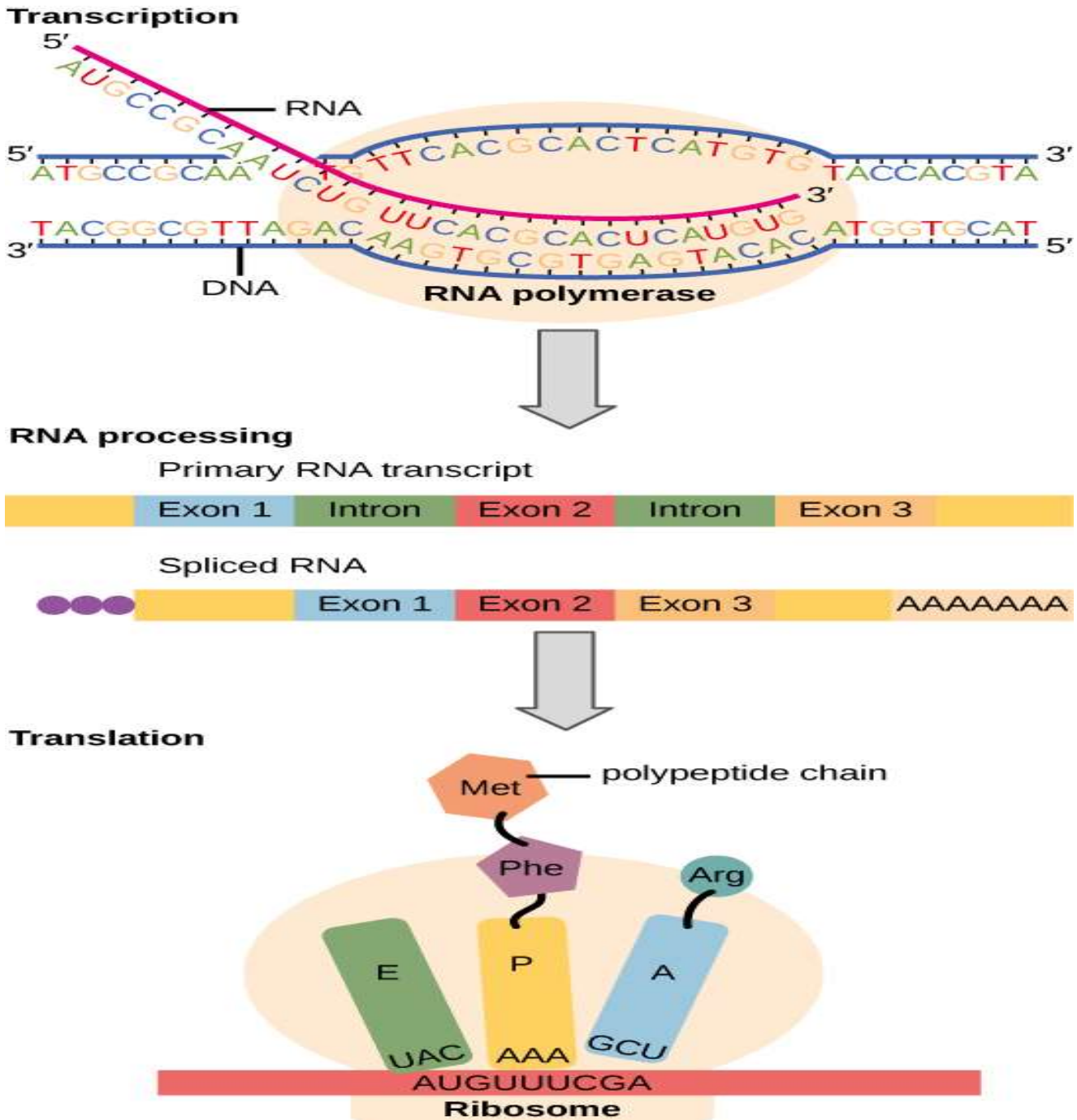
- Each tRNA molecule has an anticodon for the amino acid it carries.
- An **anticodon** is complementary to the codon for an amino acid. For example, the amino acid lysine has the codon AAG, so the anticodon is UUC. Therefore, lysine would be carried by a tRNA molecule with the anticodon UUC. Wherever the codon AAG appears in mRNA, a UUC anticodon of tRNA temporarily binds.
- While bound to mRNA, tRNA gives up its amino acid. With the help of rRNA, bonds form between the amino acids as they are brought one by one to the ribosome, creating a polypeptide chain. The chain of amino acids keeps growing until a stop codon is reached.
- Ribosomes, which are just made out of rRNA (ribosomal RNA) and protein, have been classified as ribozymes because the rRNA has enzymatic activity. The rRNA is important for the peptidyl transferase activity that bonds amino acids. Ribosomes have two subunits of rRNA and protein. The large subunit has three active sites called E, P, and A sites. These sites are important in the catalytic activity of ribosomes.

- Just as with mRNA synthesis, protein synthesis can be divided into three phases: initiation, elongation, and termination. In addition to the mRNA template, many other molecules contribute to the process of translation, such as ribosomes, tRNAs, and various enzymatic factors
- **Translation Initiation:** The small subunit binds to a site upstream (on the 5' side) of the start of the mRNA. It proceeds to scan the mRNA in the 5'-->3' direction until it encounters the START codon (AUG). The large subunit attaches and the initiator tRNA, which carries methionine (Met), binds to the P site on the ribosome.

- **Translation Elongation:** The ribosome shifts one codon at a time, catalyzing each process that occurs in the three sites. With each step, a charged tRNA enters the complex, the polypeptide becomes one amino acid longer, and an uncharged tRNA departs. The energy for each bond between amino acids is derived from GTP, a molecule similar to ATP. Briefly, the ribosomes interact with other RNA molecules to make chains of amino acids called polypeptide chains, due to the peptide bond that forms between individual amino acids. Inside the ribosome, three sites participate in the translation process, the A, P and E sites.
- **Translation Termination**: Termination of translation occurs when a stop codon (UAA, UAG, or UGA) is encountered. When the ribosome encounters the stop codon, the growing polypeptide is released with the help of various releasing factors and the ribosome subunits dissociate and leave the mRNA. After many ribosomes have completed translation, the mRNA is degraded so the nucleotides can be reused in another transcription reaction.


tRNA with first amino acid
large ribosomal subunit
small ribosomal subunit
UAC
anticodon
mRNA
5′
3′
AUG
start codon
UAG
stop codon
Components are recycled.
INITIATION
Transitional complex forms, and tRNA brings first amino acid in polypeptide chain to bind to start codon on mRNA.
ELONGATION
tRNAs bring amino acids one by one to add to polypeptide chain.
TERMINATION
Release factor recognizes stop codon, translational complex dissociates, and completed polypeptide is released.
release factor
completed polypeptide
UAC
AUG
UAG
stop codon

After a polypeptide chain is synthesized, it may undergo additional processes. For example, it may assume a folded tertiary shape due to interactions among its amino acids. It may also bind with other polypeptides or with different types of molecules, such as lipids or carbohydrates. Many proteins travel to the Golgi apparatus within the cytoplasm to be modified for the specific job they will do.


Transcription
5′
RNA
5′
3′
3′
3′
5′
DNA
RNA polymerase
RNA processing
Primary RNA transcript
Exon 1
Intron
Exon 2
Intron
Exon 3
Spliced RNA
Exon 1
Exon 2
Exon 3
AAAAAAA
Translation
Met
polypeptide chain
Phe
Arg
E
P
A
UAC
AAA
GCU
AUGUUUCGA
Ribosome

# PATTERN OF INHERITANCE

# TERMINOLOGIES

- **Gene: -** A gene is a stretch of DNA or RNA that determines a certain trait.
- **Allele: -** An allele is a variant form of a given gene.
- **Phenotype: -** It is the composite of the organisms observable characteristics including its morphology, its developmental process, its biochemical and physiological properties.
- **Chromosome: -** A threadlike structure of nucleic acids and protein found in the nucleus of most living cells, carrying genetic information in the form of genes.
- **Dominant: -** It is one that always produces a particular characteristics in a person, plant or animal

- **Recessive: -** It is a gene that can be masked by a dominant gene.
- **Gamete: -** They are sex cells that unite during sexual reproduction to form a new cell called a zygote.
- **Homozygous: -** Having two identical alleles of a gene
- **Heterozygous: -** Having two different alleles of a gene
- **Polygenetic : -** Having more than one origin or source.

# WHAT IS INHERITANCE?

Genetic trait or characteristics that is passed on from a parent to the next generation of offspring.

# MENDELIAN THEORY OF INHERITANCE

- Gregor Johann Mendel was born on July 22, 1822 in Austria.
- He was the only son of a peasant farmer.
- During the middle of Mendel’s life, Mendel did ground breaking work into the theories of heredity. Using simple pea plant, Mendel studied seven basic characteristics of the pea plants.
- By tracing these characteristics, Mendel discovered three basic laws, which governed the passage of a trait from one member of a species to another member of the same species.

1. The **FIRST LAW** states that the sex cells of a plant may contain two different traits, but not both of those traits.
2. The **SECOND LAW** stated that the characteristics are inherited independently from another
3. The **THIRD LAW** states that each inherited characteristics is determined by two hereditary factors, one from each parents, which decides whether a gene is dominant or recessive.

# LAWS OF INHERITANCE

Mendel has given three laws of inheritance, which are follows:

1. **Law of dominance**
2. **Law of segregation**
3. **Law of independent assortment**

# 1. LAW OF DOMINANCE

- Out of the pair of contrasting characters present together, only one is able to express itself while the other remained suppressed.
- The one that express is the dominant character and the one unexpressed is the recessive character.
- The recessive character can be expressed only when the pair consists of both the recessive traits.

# 2. LAW OF SEGREGATION

- It is also called law of purity of gametes, “The two members of a pair of factors separate during the formation of gametes”.
- They do not blend but segregate or separate during the formation of gametes. The gametes combine together by random fusion at the time of zygote formation.

# 3. LAW OF INDEPENDENT ASSORTMENT

When there are two pairs of characters, “the distribution of the alleles of one character into the gametes is independent of distribution of the alleles of the other character.

# TYPES OF INHERITANCE

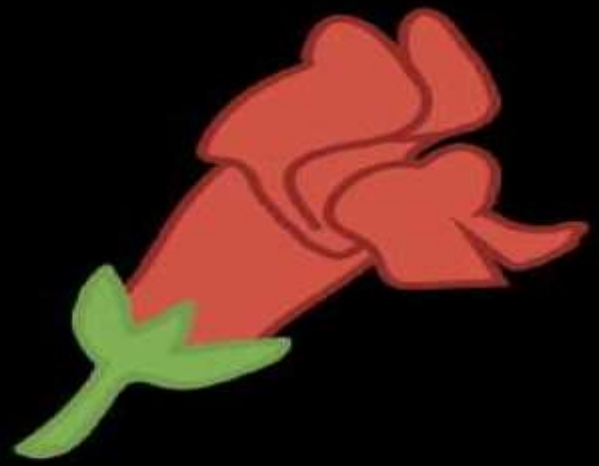
- Dominant – recessive
- Incomplete dominance
- Co-dominant
- Sex-limited
- Sex-linked

# DOMINANT – RECESSIVE

- If both or one of the gametes are dominant, the dominant trait is inherited by the offspring.
- When one or both alleles is dominant the organism has the dominant trait
- When it is a homozygous with recessive alleles, it has the recessive trait

# INCOMPLTETE DOMINANCE

- When neither allele has dominance over the other allele
- The offspring would result as an intermediate of the two homozygous parental phenotype, and would therefore be a heterozygous
- Ex: a pink flower would result when red and white flowers breed.



# CO-DOMINANT

- When both alleles in a heterozygous organism contribute to phenotype
- Both alleles are independently and equally expressed.
- Ex: When a red bull and white cow breed a roan coloured cow would result.

# SEX-LIMITED

- Cannot be identified with phenotype.
- Some characteristics unique to the sex will not be passed on, such as milking characteristics of female not being passed on to male.

# SEX-LINKED

- Highly dependent on the x chromosome
- X chromosome acts a recessive allele
- XX makes female, XY makes male

# POLYGENITIC INHERITANCE

- Single characteristics controlled by multiple genes.

# POLYGENIC INHERITANCE IN SKIN COLOR

- Gives rise to continuous variation in phenotype
- Polygenic alleles can be contributing or non-contributing
- The genotype varies due to segregation of alleles and unlinked chromosomes orienting randomly, and random fertilization of gametes
- In total 9 genotypes are possible