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DNA function: gene expression

Modul no. 1: Animal Genetics

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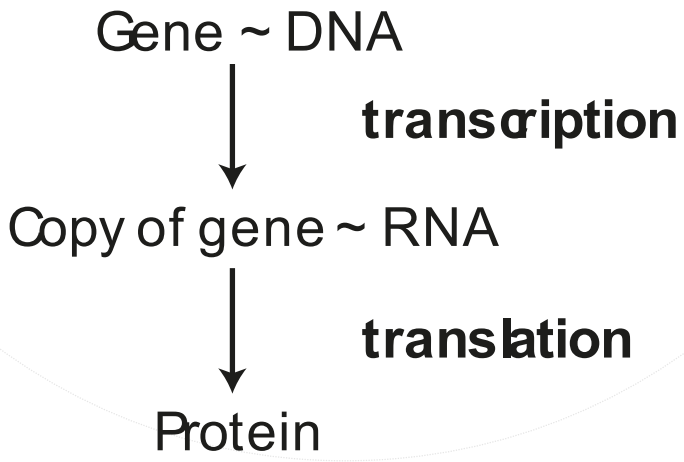
Gene and its expression

- Genes contain biological information, but on their own they are unable to release that information to the cell. Its utilization requires the coordinated activity of enzymes and other kinds of proteins, which participate in the series of events that make up gene expression.
- Gene expression is conventionally described as a two-stage process.
- All these processes are based on the structural properties of nucleic acids: base complementarity and antiparallelism in double-helical NK structures.



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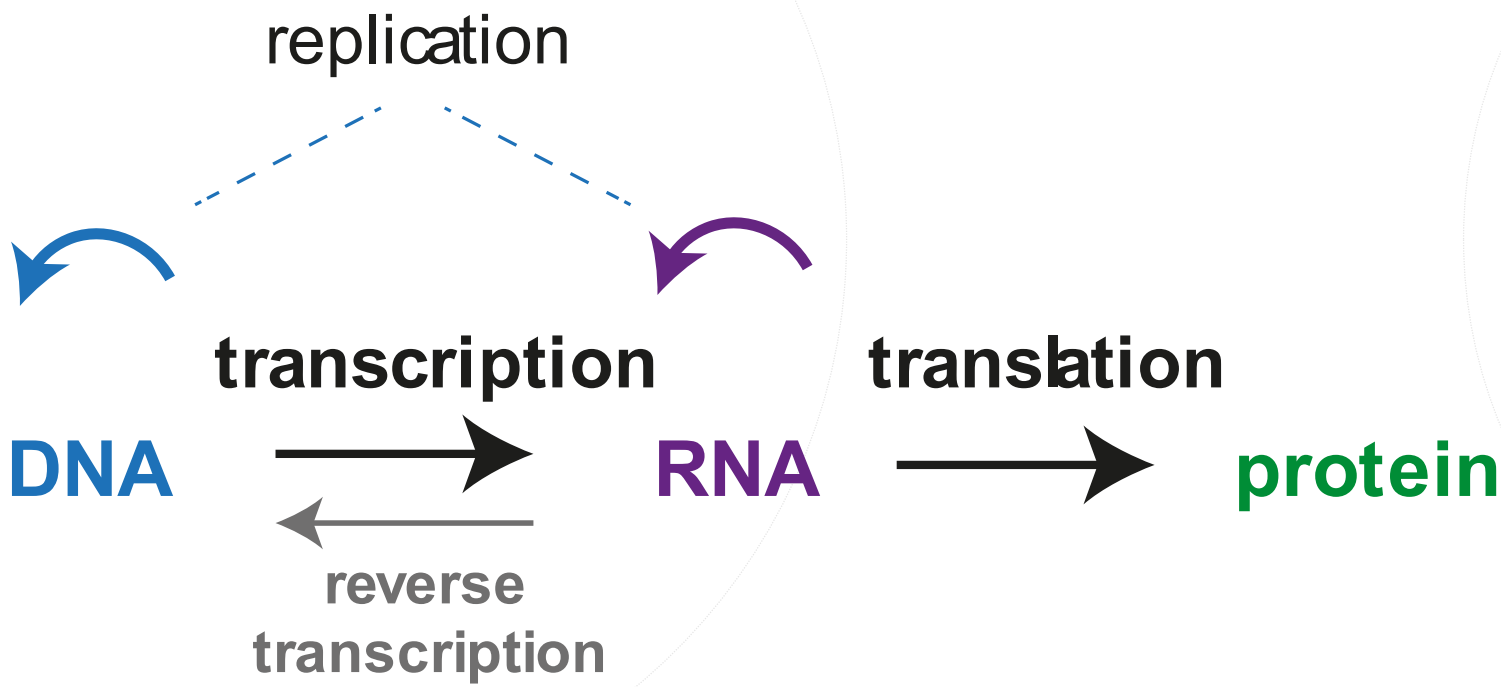
Function of DNA – Dogma of molecular biology

- The flow of genetic information in the cell ~ the central dogma of molecular biology



- GI transfer between nucleic acids and from NK to protein is possible, but not from protein to NK

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Expression of genetics information

- Gene expression is the process by which information from a gene is used in the synthesis of a functional gene product that enables it to produce end products, protein or non-coding RNA.
- The expression of genetic information is a process involving two steps
  - **transcription**
  - **translation**
- During these processes, proteins are created - the basis of the correct phenotype.

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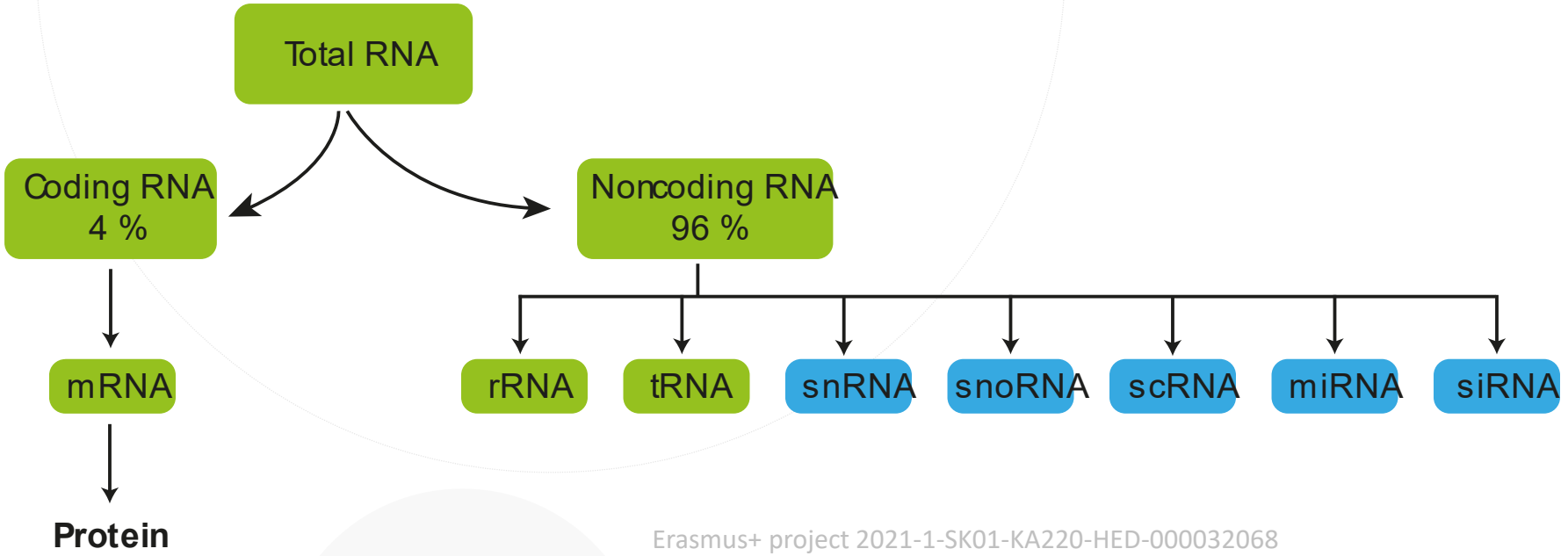
RNA molecules

- The RNA molecules that are not translated into protein are also important
- messenger RNA (mRNA) is about 4%
- the remaining proportion is made up of non-coding RNA with its own function:

  small nuclear RNA (snRNA), small nucleolar RNAs (snoRNAs), small cytoplasmic RNAs (scRNAs), microRNAs (miRNAs), and small interfering RNAs (siRNAs)



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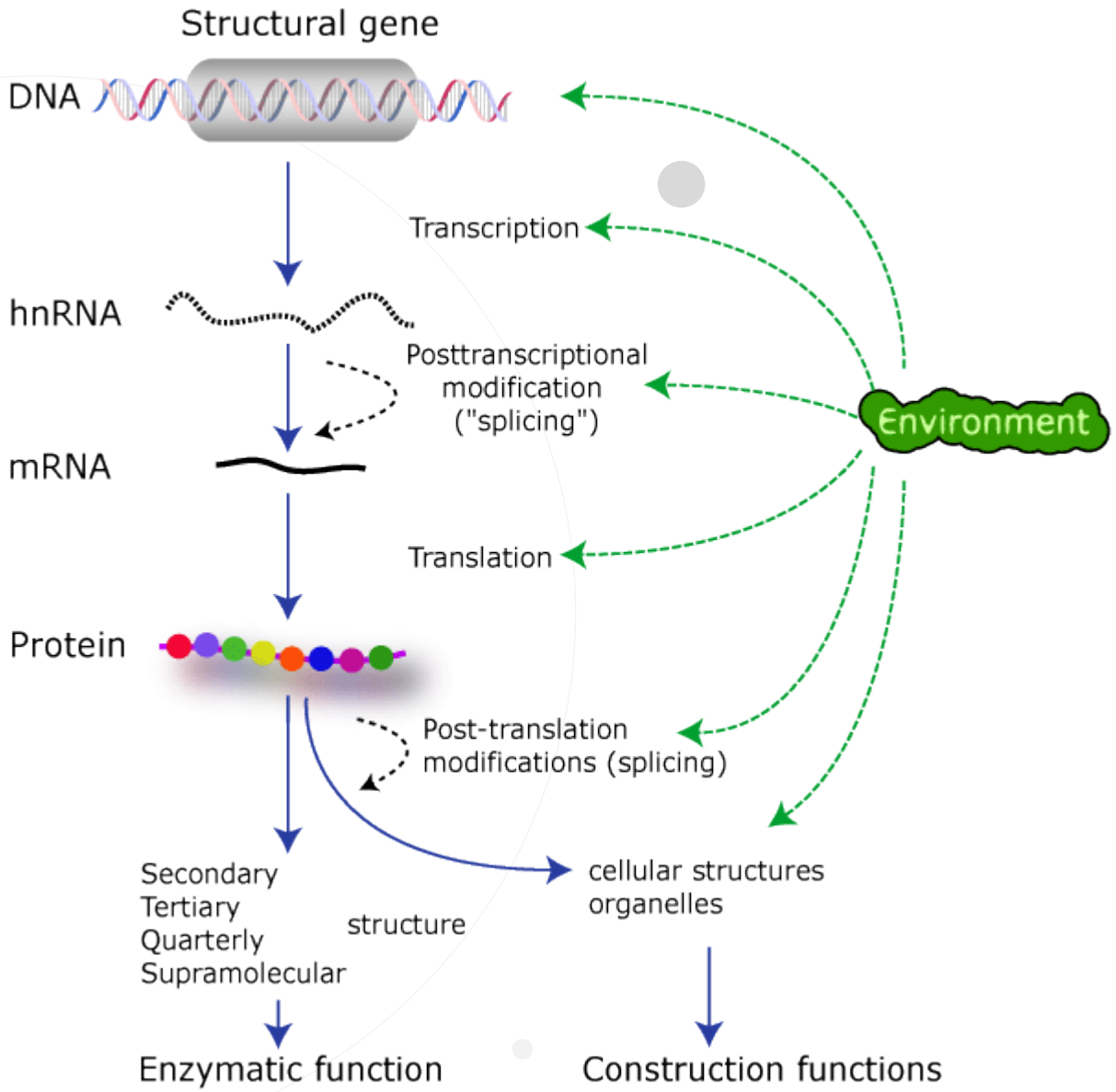

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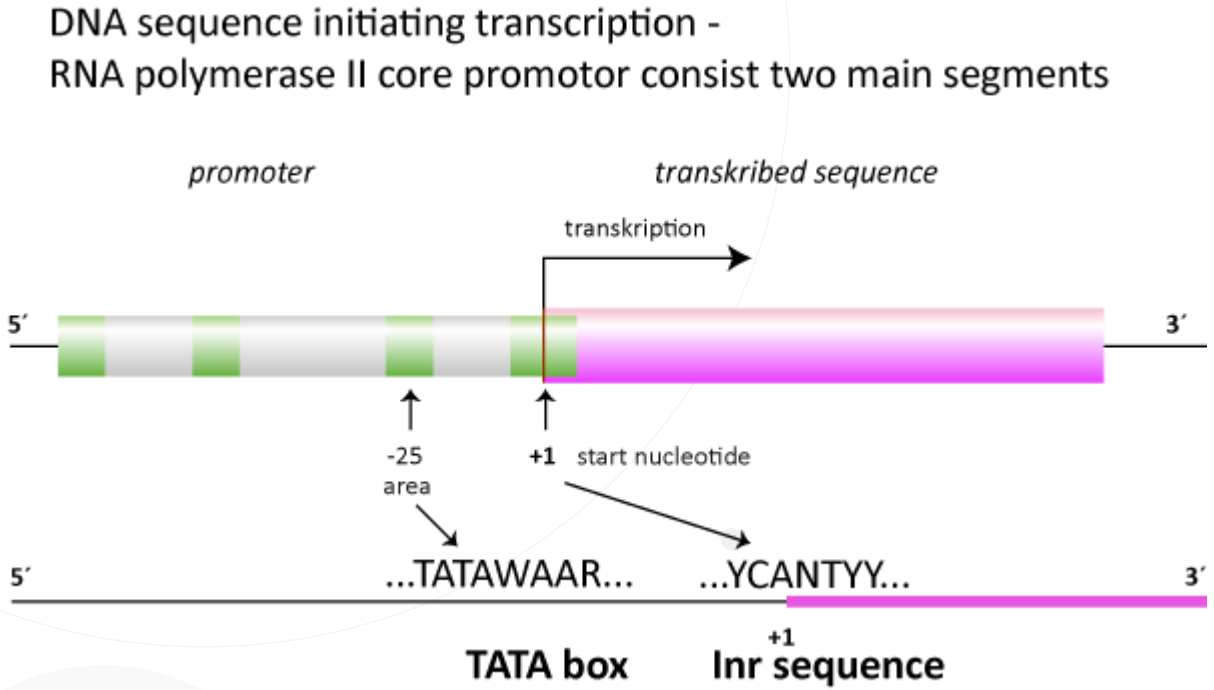
Promoter

- a promoter is a sequence of DNA that initiates the transcription of a particular gene by binding RNA polymerase or other components of the transcription machinery
- In eukaryotes, there are three types of RNA polymerase (I - III), each with specific promoters.
- The RNA polymerase II core promoter in eucaryotes consists of two main segments.
  - **TATA box**, pos. –25 with consensus sequence 5'-TATAWAAR-3'.
  - **initiator** (**Inr**) **sequence**, which is located around nucleotide +1 (in mammals)



W ~ A/T
R ~ A/G
Y ~ C/T
N ~ A/G/C/T

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Transkription

- The result of transcription is the synthesis of an RNA molecule based on complementarity with DNA.
- RNA, like DNA, is a polynucleotide, the only chemical differences being that in RNA the sugar is ribose rather than 2’-deoxyribose, and that the base thymine is replaced by the base uracil (U), which, like thymine, base-pairs with adenine.
- During transcription of a gene, one strand of the DNA double helix acts as a template for synthesis of an RNA molecule.

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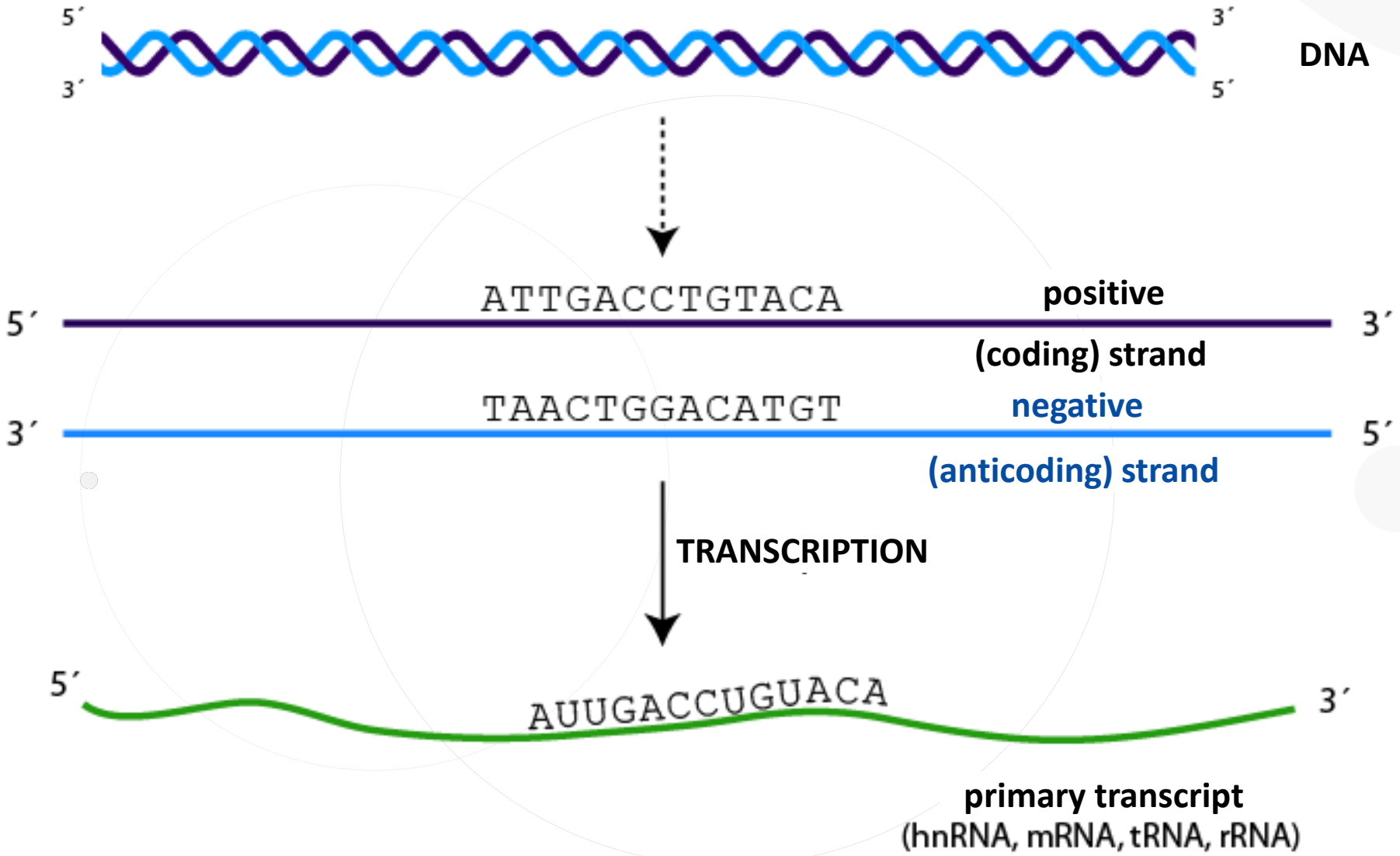

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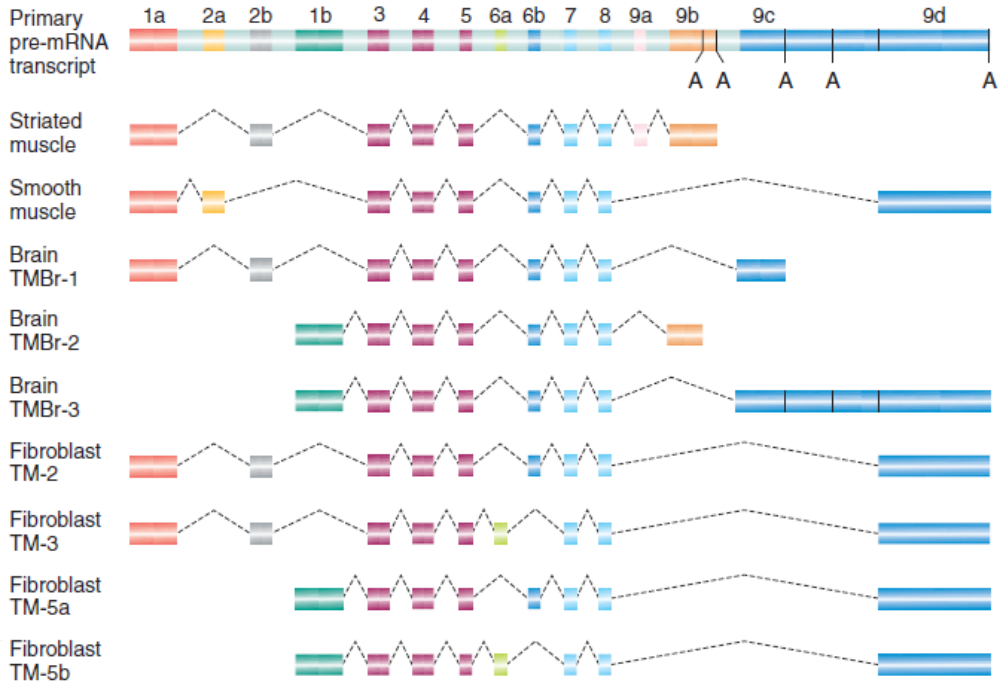
Processing after RNA synthesis

- Capping
- **RNA splicing**, the removal of introns
- Cleavage and polyadenylation

The pre-mRNA transcript of the rat alfa-tropomyosin gene is **alternatively spliced** in different cell types. The light green boxes represent introns; the other colors represent exons. Polyadenylation signals are indicated by an A. Dashed lines in the mature mRNAs indicate regions that have been removed by splicing.

Complex patterns of eukaryotic mRNA splicing



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Translation

- In the case of structural genes, the mRNA undergoes the second phase of gene expression – translation
- Translation of genetic information (nucleotide sequence) into the primary polypeptide structure (amino acid sequence)
- In a protein, the monomers are called amino acids, and there are 20 different ones, each with its own specific chemical properties.

- **Principle**: through base complementarity between the mRNA codon (gene copy) and the tRNA anticodon (amino acid carrier)
- It uses the genetic code - a system of amino acid coding rules
- Translation takes place on ribosomes in the cytoplasm

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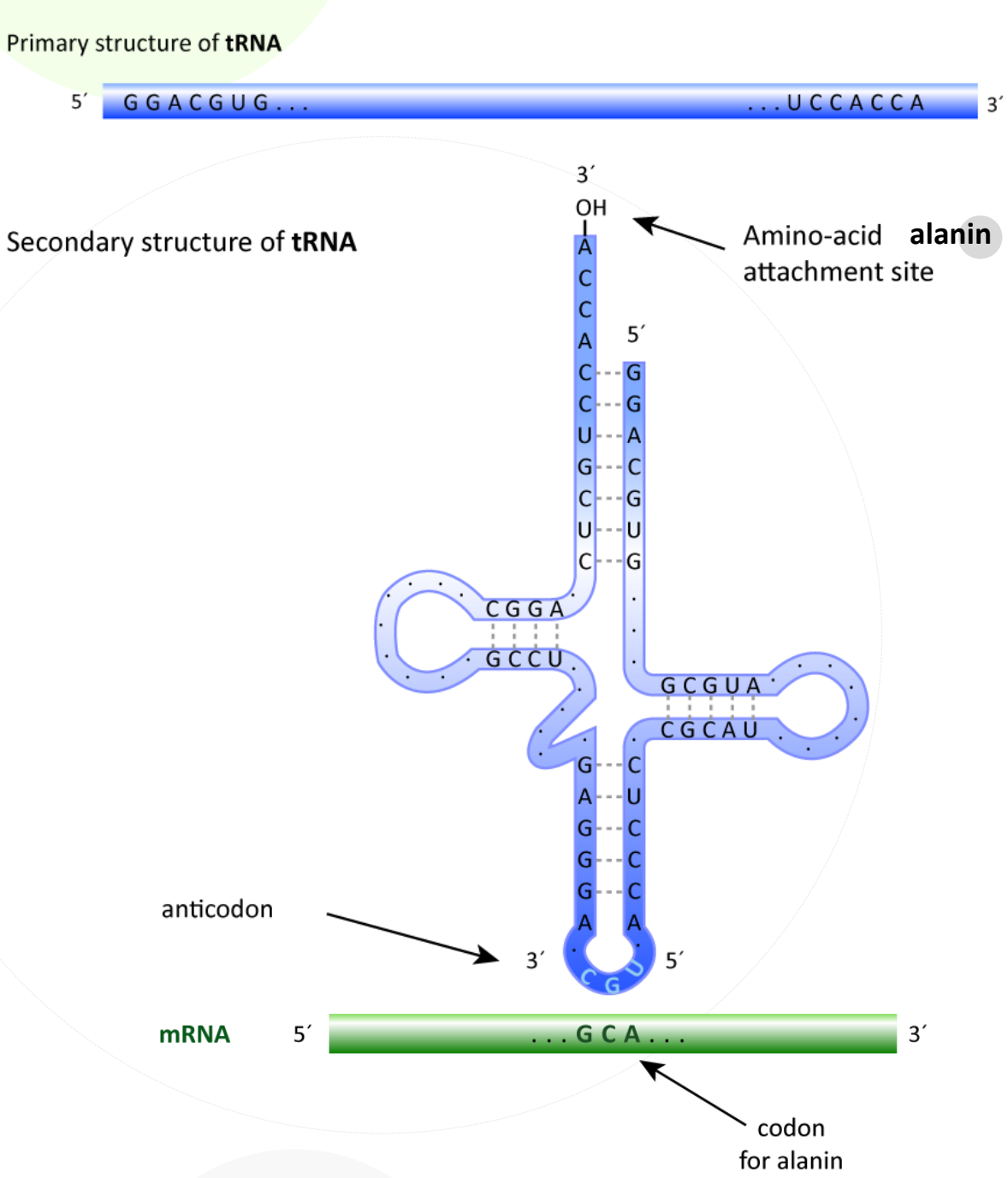
Codon – anticodon pairing



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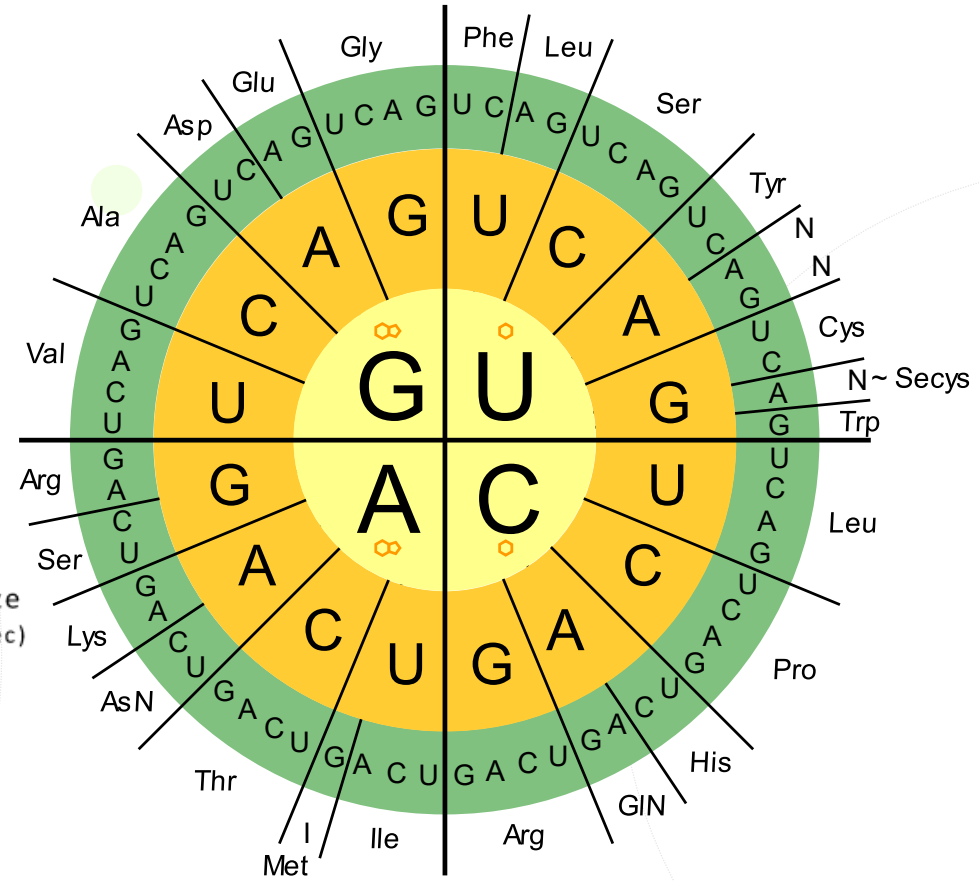
Genetic code

1. báze (5´konec) \ 2. báze	U	C	A	G	3. báze (3´konec)
U	Phe UUU	Ser UCU	Tyr UAU	Cys UGU	U
	Phe UUC	Ser UCC	Tyr UAC	Cys UGC	C
	Leu UUA	Ser UCA	Stop UAA	Stop* UGA	A
	Leu UUG	Ser UCG	Stop UAG	Trp UGG	G
C	Leu CUU	Pro CCU	His CAU	Arg CGU	U
	Leu CUC	Pro CCC	His CAC	Arg CGC	C
	Leu CUA	Pro CCA	Gln CAA	Arg CGA	A
	Leu CUG	Pro CCG	Gln CAG	Arg CGG	G
A	Ile AUU	Thr ACU	Asn AAU	Ser AGU	U
	Ile AUC	Thr ACC	Asn AAC	Ser AGC	C
	Ile AUA	Thr ACA	Lys AAA	Arg AGA	A
	Met I AUG	Thr ACG	Lys AAG	Arg AGG	G
G	Val GUU	Ala GCU	Asp GAU	Gly GGU	U
	Val GUC	Ala GCC	Asp GAC	Gly GGC	C
	Val GUA	Ala GCA	Glu GAA	Gly GGA	A
	Val GUG	Ala GCG	Glu GAG	Gly GGG	G

I - Iniciační kodon; * - Sec - Selenocystein ; Stop - Terminační (stop) kodon



The sequence of amino acids is determined by the sequence of nucleotides in the mRNA. Each triplet of contiguous ribonucleotides specifies one amino acid of the protein, with the identity of the amino acid corresponding to each triplet being given by the genetic code.

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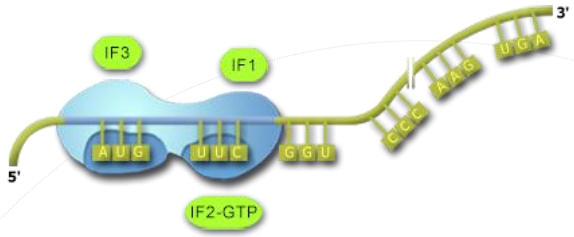
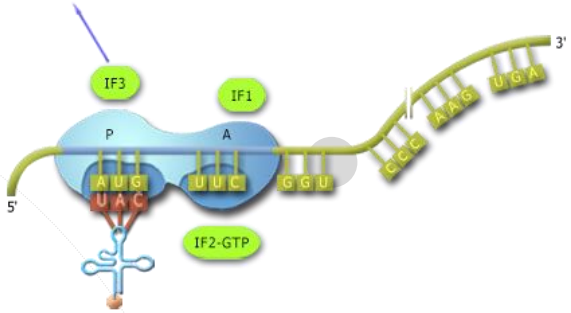
TRANSLATION



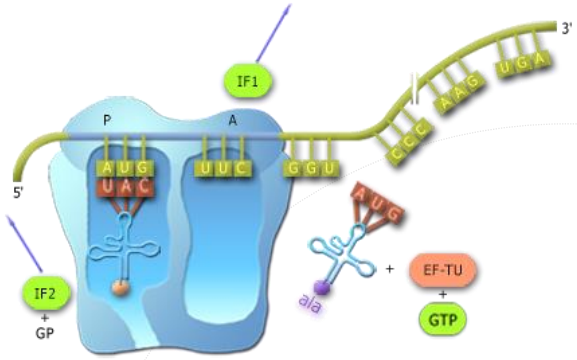
1. mRNA binds to small ribosomal subunit with initiation factors (IF1, 2 a 3)

TRANSLATION



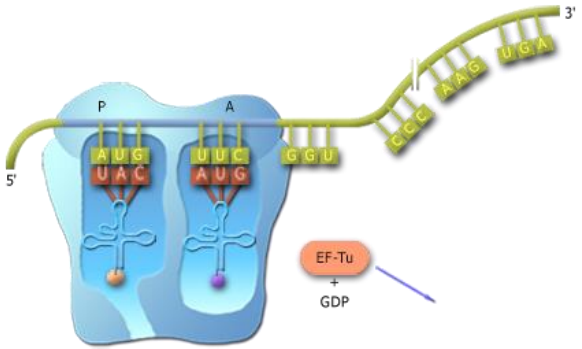
2. Initiator fMet-tRNA binds to codon sequence mRNA with its anticodon on site P - initiation complex; IF3 is released

TRANSLATION



3. After IF3 is released, the big subunit joins the initiation complex; GTP is cleaved and IF-1 and IF-2 are released. Elongation fator EF-Tu binds to subsequent aminoacyl-tRNA.

TRANSLATION



4. Phe-tRNA enters A site of ribosome to the exposed codon UUC and EF-Tu is released.

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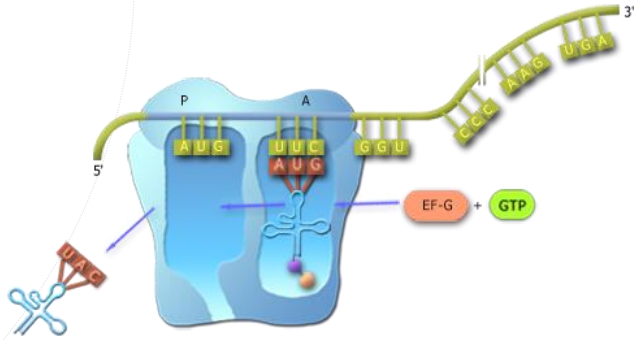

5. Peptide bond forms between the two adjacent amino acids, catalised by peptidyl transferase. The linked amino acids are attached to the tRNA in the A site, forming a peptidyl-tRNA. Translocation occures as the ribosome moves one codon to the right and peptidyl-tRNA moves from the A site to the P site. Uncharged tRNA is released.

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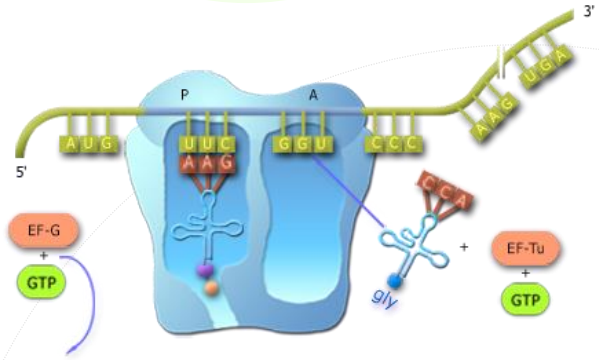
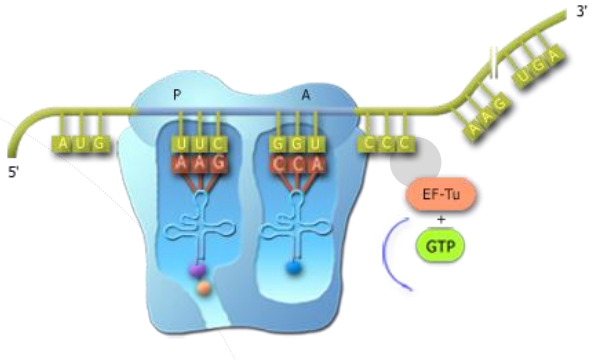
TRANSLATION



6. When translocation is complete and the peptidyl-tRNA is in P site and ribosome is ready for another elongation cycle.

TRANSLATION



7. The third activated tRNA with amino acid Gly enters into the A site...

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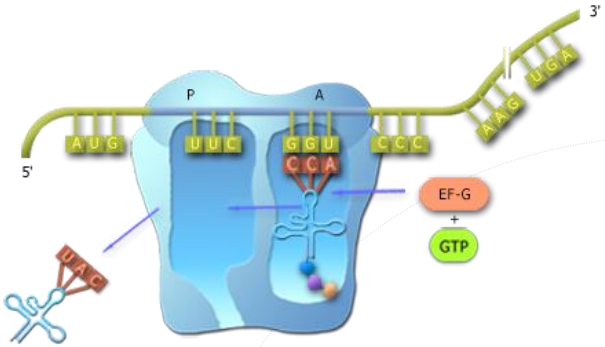

8. Polypeptide grow up another amino acid.

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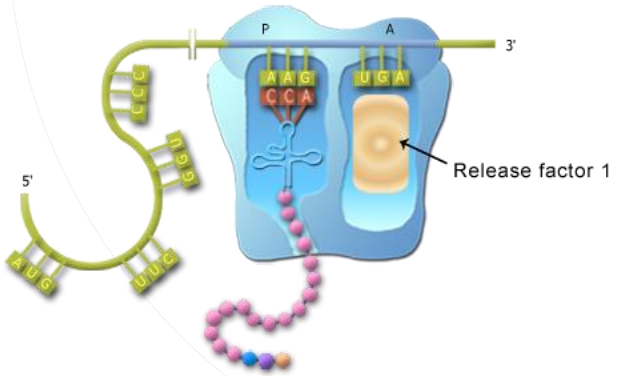

9. The elongation cycles repeats until stop codon UGA is encountered.Release factor 1 binds to the UGA termination codon in the A site.

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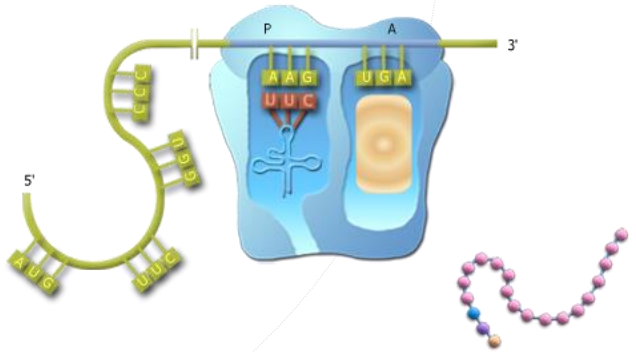
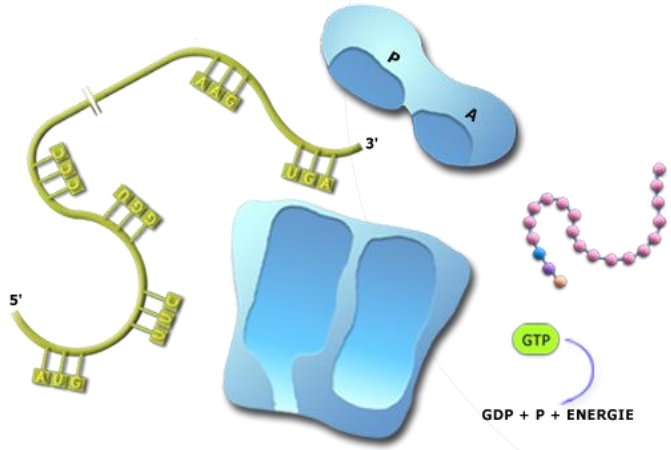


10. Polypeptide chain is released.

TRANSLATION



11. Release of the nascent polypeptide, tRNA, ribosome complex, RF-1 and mRNA.

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