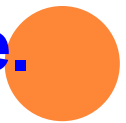


# Transcription



- ⊙ **Transcription is a process in which ribonucleic acid (RNA) is synthesized from DNA.**
- ⊙ **Gene refers to the functional unit of DNA that can be transcribed.**
- ⊙ **The genetic information stored in DNA is expressed through RNA.**
- ⊙ **One of the two strands of DNA serves as a template (non-coding strand or sense strand) & produces working copies of RNA molecule.**



- ◎ **The other DNA strand which does not participate in transcription is referred to as coding strand or antisense strand (frequently referred to as coding strand since with the exception of T for U, primary mRNA contains codons with the same base sequence.**



# Transcription is selective

- ⊙ **The entire molecule of DNA is not expressed in transcription.**
- ⊙ **RNAs are synthesized only for some selected regions of DNA.**
- ⊙ **For certain other regions of DNA, there may not be any transcription at all.**
- ⊙ **The product formed in transcription is referred to as primary transcript.**



- ⊙ **The primary RNA transcripts are inactive.**
- ⊙ **They undergo certain alterations (splicing, terminal additions, base modifications etc.) commonly known as post-transcriptional modifications, to produce functionally active RNA molecules.**



# Transcription in Prokaryotes

- ⦿ A single enzyme-DNA dependent RNA polymerase or RNA polymerase synthesizes all the RNAs in prokaryotes.



# Stages

- ⊙ Transcription involves three different stages- initiation, elongation & termination.
- ⊙ **Initiation:**
- ⊙ **The binding of the enzyme RNA polymerase to DNA is the prerequisite for the transcription to start.**
- ⊙ **The specific region on the DNA where the enzyme binds is known as promoter region.**

- ⊙ **There are two base sequences on the coding DNA strand which the sigma factor of RNA polymerase can recognize for initiation of transcription.**
- ⊙ **Pribnow box (TATAbox):**
- ⊙ **This consists of 6 nucleotide bases (TATAAT), located on the left side about 10 bases away (upstream) from the starting point of transcription.**

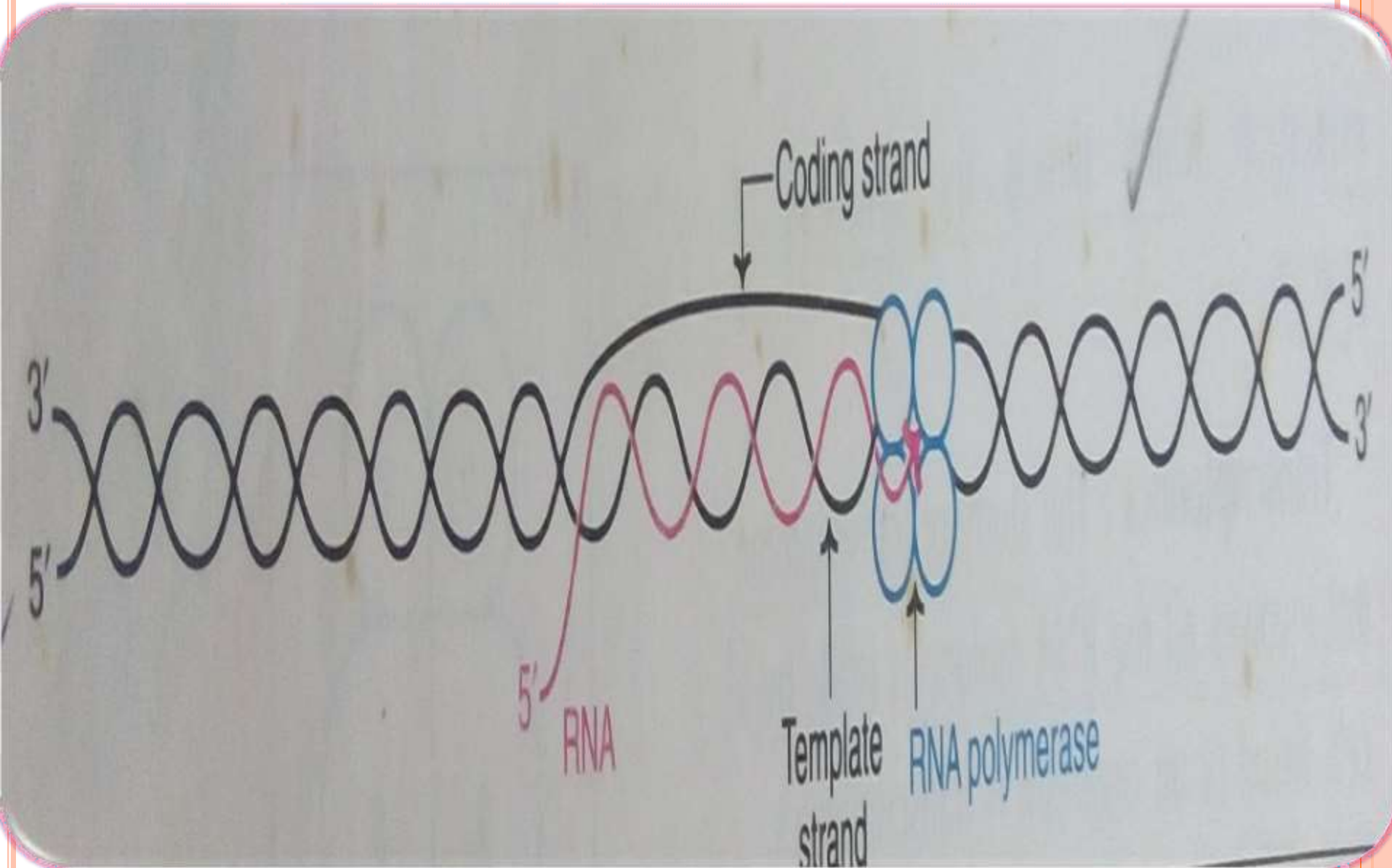




- ◎ **The '-35' sequence:**
- ◎ **This is the second recognition site in the promote region of DNA.**
- ◎ **It contains a base sequence TTGACA, which is located about 35bases (upstream, hence - 35) away on the left side from the site of transcription start.**



# Transcription



# Elongation

- ⊙ **As the holoenzyme, RNA polymerase recognizes the promoter region, the sigma factor is released & transcription proceeds.**
- ⊙ **RNA is synthesized from 5' end to 3' end (5'-3') antiparallel to the DNA template.**
- ⊙ **RNA polymerase utilizes ribonucleotide triphosphates (ATP, GTP, CTP & UTP) for the formation of RNA.**



- ⊙ **For the addition of each nucleotide to the growing chain, a pyrophosphate moiety is released.**
- ⊙ **The sequence of nucleotide bases in the mRNA is complementary to the template DNA strand.**
- ⊙ **It is identical to that of coding strand except that RNA contains U in place of T in DNA.**



- ⊙ **RNA polymerase differs from DNA polymerase in two aspects.**
- ⊙ **No primer is required for RNA polymerase & this enzyme does not possess endo – or exonuclease activity.**
- ⊙ **Due to lack of proof-reading activity, RNA polymerase has no ability to repair the mistakes in the RNA synthesized.**



# Termination

- ⦿ The process of transcription stops by termination signals.
- ⦿ Two types of termination are identified.
- ⦿ Rho (p) dependent termination.
- ⦿ Rho (p) independent termination.




# Rho ( $\rho$ ) dependent termination

- ⊙ A specific protein –  $\rho$  factor, binds to growing RNA (& not to RNA polymerase) or weakly to DNA, & in the bound state it acts as ATPase & terminates transcription & releases RNA.
- ⊙ The  $\rho$  factor is also responsible for the dissociation of RNA polymerase from DNA.



## Rho ( $\rho$ ) independent termination

- ⊙ This is due to the formation of hairpins of newly synthesized RNA.
  - ⊙ This occurs due to the presence of palindromes.
  - ⊙ A palindrome is a word that reads a like forward & backward. e.g. madam, rotor.
- 



- ⊙ **The presence of palindromes in the base sequence of DNA templates (same when read in opposite direction) in the termination.**
- ⊙ **As a result of this, the newly synthesized RNA folds to form hairpins (due to complementary base pairing) that cause termination of transcription.**



# Transcription in Eukaryotes

- ⊙ **RNA polymerases:**
- ⊙ **The nuclei of eukaryotic cells possess three distinct RNA polymerases.**
- ⊙ **RNA polymerase I** is responsible for the synthesis of precursors for the large ribosomal RNAs.
- ⊙ **RNA polymerase II** synthesizes the precursors for mRNAs & small nuclear RNAs.

- ⊙ **RNA polymerase III** participates in the formation of tRNAs & small ribosomal RNAs.
- ⊙ **A mitochondrial RNA polymerase.**



## Promoter sites

- ⊙ **In eukaryotes**, a sequence of DNA bases which is almost identical to pribnow box of prokaryotes.
- ⊙ **This sequence**, known as Hogness box (or **TATAbox**), is located on the left about 25 nucleotides away (upstream) from the starting site of mRNA synthesis.



- ⊙ **There also exists another site of recognition between 70&80 nucleotides upstream from the start of transcription.**
- ⊙ **This second site is referred to as CAAT box.**
- ⊙ **One of these two sites (or sometimes both) helps RNA polymerase II to recognize the requisite sequence on DNA for transcription.**



# Initiation of transcription

- 1. Chromatin containing the promoter sequence made accessible to the transcription machinery.**
- 2. Binding of transcription factors (TFs) to DNA sequences in the promoter region.**
- 3. Stimulation of transcription by enhancers.**



# Heterogeneous nuclear RNA (hnRNA)

- ⊙ The **primary mRNA transcript** produced by RNA polymerase II in eukaryotes is often referred to as **heterogeneous nuclear RNA (hnRNA)**.
- ⊙ This is then processed to produce mRNA needed for protein synthesis.



# Post-transcriptional modifications

- ⊙ **The primary transcripts undergo many alterations-terminal base additions, base modifications, splicing etc, which are collectively referred to as post-transcriptional modifications.**
- ⊙ **This process is required to convert the RNAs into the active forms.**





- ⊙ **A group of enzymes – ribonucleases are responsible for the processing of tRNAs & rRNAs of both prokaryotes & eukaryotes.**
- ⊙ **The prokaryotic mRNA synthesized in transcription is almost similar to the functional mRNA.**
- ⊙ **In contrast, eukaryotic mRNA (i.e. hnRNA) undergoes extensive post-transcriptional changes.**



# Messenger RNA

- ⊙ **The 5' capping:**
- ⊙ **The 5' end of mRNA is capped with 7-methylguanosine by an unusual 5'-5' triphosphate linkage.**
- ⊙ **This cap is required for translation, besides stabilizing the structure of mRNA.**



- ⊙ **Poly-A tail:**
- ⊙ **A large number of eukaryotic mRNAs possess an adenine nucleotide chain at the 3'-end.**
- ⊙ **Poly-A tail is not produced during transcription.**
- ⊙ **It is later added to stabilize mRNA.**
- ⊙ **Poly-A chain gets reduced as the mRNA enters cytosol.**



- ⦿ **Introns & their removal:**
- ⦿ **Introns are the intervening nucleotide sequences in mRNA which do not code for proteins.**
- ⦿ **Exons of mRNA possess genetic code and are responsible for protein synthesis.**



- ◎ **The removal of introns is promoted by small nuclear ribo-nucleoprotein particles (snRNPs).**



- ⦿ **Post-transcriptional modifications of mRNA occur in the nucleus.**
- ⦿ **The mature RNA then enters the cytosol to perform its function (translation).**



# Faulty splicing can cause diseases

- ⊙ Faulty splicing may result in diseases.
- ⊙ Example is one type of  $\beta$ -thalassemia.
- ⊙ Mutation that results in a nucleotide change at an exon-intron junction.
- ⊙ The result is a diminished or lack of synthesis of  $\beta$ -chain of hemoglobin



# Transfer RNA

- ⊙ **All the tRNAs of prokaryotes & eukaryotes undergo post-transcriptional modification.**
- ⊙ **These include trimming, converting the existing bases into unusual ones & addition of CCA nucleotides to 3' terminal end of tRNAs.**





# Ribosomal RNA

- ⊙ **The preribosomal RNAs originally synthesized are converted to ribosomal RNAs by a series of post-transcriptional changes.**



# Inhibitors of transcription

- ⊙ **Actinomycin D:**
- ⊙ **This is also known as dactinomycin.**
- ⊙ **It is synthesized by Streptomyces.**
- ⊙ **Actinomycin D binds with DNA template strand & blocks the movement of RNA polymerase.**
- ⊙ **This was the very first antibiotic used for the treatment of tumors.**



- ⊙ **Rifampin:**
- ⊙ **It is an antibiotic widely used for the treatment of tuberculosis and leprosy.**
- ⊙ **Rifampin binds with the  $\beta$ -subunit of prokaryotic RNA polymerase & inhibits its activity.**



- ⊙  **$\alpha$ -Amanitin:**
- ⊙ **It is a toxin produced by mushroom,**
- ⊙ **This mushroom is delicious in taste but poisonous due to the toxin  $\alpha$ -amanitin which tightly binds with RNA polymerase II of eukaryotes & inhibits transcription.**



# Reverse transcription

- ⊙ **Retroviruses possess RNA as the genetic material.**
- ⊙ **These viruses cause cancers in animals, hence known as **oncogenic**.**
- ⊙ **They are actually found in the transformed cells of the tumors.**

