[PDF] Inhibitors of Transcription and Translation Notes

This blog involves information about Inhibitors of Transcription and Translation separately as Inhibitors of transcription in prokaryotes and Inhibitors of transcription in eukaryotes. before we directly jump into the List of inhibitors of translation and learn about Inhibitors of transcription in prokaryotes and Inhibitors of transcription in eukaryotes let us revise the process of transcription and translation. This will help us in understanding the mechanism of the inhibitor.

Introduction:

DNA is the blueprint of life as it consists of all the genetic information of an individual. When DNA codes proteins in three steps like replication, transcription and translation it forms the central dogma of molecular biology. The 'Central Dogma' is the operation by which the information in DNA is remade into an applicable product. It was foremost proposed in 1958 by Francis Crick, discoverer of the structure of DNA. Inhibitors of Transcription and Translation are the drugs that stop the central dogma process. Which has become an important point not just in the field of molecular biology but also in medical science.

Transcription:

The process of copying genetic information from one strand of DNA into RNA is termed transcription. It occurs unidirectionally in which RNA is synthesized from the 5' to 3' direction.

TRANSCRIPTION UNIT:

Transcription is a selective process. Each transcribed segment of DNA is called a transcription unit. A transcription unit consists of,

i) A promoter.

ii) The structural gene.

iii) A Terminator.

In eukaryotes, a transcription unit typically carries the information of just one gene and it is termed a monocistronic transcription unit. In prokaryotes, a set of adjacent genes is often transcribed as a unit termed polycistronic transcription unit The immediate product of transcription is called the primary transcript. The eukaryotic transcription unit may be simple or complex. The primary transcript produced from a simple transcription unit is processed to yield a single type of mRNA, encoding a single protein. In the case of complex transcription units, which are quite common in multicellular organisms, the primary RNA transcript can be processed in more than one way, leading to the formation of more than one type of mRNAs, encoding more than one type of polypeptides. Transcription starts from the first base pair that is called the start point. From this point, RNA polymerase moves along the template, synthesizing RNA, until it reaches a terminator sequence. Sequences prior to the start point are described as upstream of it those after the start point (within the transcribed sequence) are downstream of it.

Process of transcription

Initiation

Initiation of transcription describes the formation of a first phosphodiester bond between two nucleotides in an RNA. RNA polymerase as a holoenzyme binds at the promoter and starts the initiation reaction by forming a closed binary complex. Closed means that the DNA remains duplex. Sigma factor confers the ability to recognize consensus sequence within the promoter. The core enzyme does not distinguish between promoters and other sequences of DNA. Sigma factor changes the DNA-binding properties of RNA polymerase so that its affinity for promoters is increased and reduced for other sequences of DNA. Promoter structure determines the basal level of transcription initiation.

Elongation

Elongation involves the movement of the transcription bubble by a disruption of DNA structure. The enzyme moves along the DNA and extends the growing RNA chain. As the enzyme moves, it unwinds the DNA helix to expose a new segment of the template in single-stranded conditions.

Termination

It involves recognition of the point at which no further bases should be added to the chain. The sequence of DNA required for these reactions is called the terminator At this point, the enzyme stops adding nucleotides to the growing RNA chain, releases the completed product and dissociates from the DNA template.

TRANSLATION:

- **Activation**: The mRNA codes for a particular protein by the process of Translation. In the process, the ribosome translates the mRNA produced from DNA into a chain of specific amino acids. which involves the Charging of tRNA.
- **Initiation**: It involves the recognition of start codon and then binding of ribosomal subunits to mRNA while formation of initiation complex with Met-tRNA at the P-site. For initiation, the ribosome binds to the mRNA at the start codon (AUG) which is recognised only by the initiator tRNA.
- **Elongation**: After the activation and initiation process theelongation takes place by Peptide bond formation and growing of polypeptide chain. The ribosome proceeds to the elongation phase of protein synthesis. During this stage, complexes of an amino acid linked to tRNA, sequentially bind to the appropriate codon in mRNA by forming complementary base pairs with the tRNA anticodon. The ribosome moves from codon to codon along the Amino acids are added one by one, translated into polypeptide sequences dictated by DNA and represented by mRNA.
- **Termination**: For the termination of transaltion process stop codon enters the A site which then resulting in the termination of the process. So In the end, a release factor binds to the stop codon, terminating translation and releasing the complete polypeptide from the ribosome.

INHIBITORS OF TRANSCRIPTION

1. **Streptolydigin**:

It blocks the nucleic acid chain elongation by binding to the polymerase and thereby stops the RNA polymerase activity inside the cell.

2. Rifampicin (rifamycin):

It is an antibiotic used to treat tuberculosis. It binds to the beta subunit of bacterial RNA polymerase and inhibits mitochondrial RNA polymerase.

3. Alpha amanitin:

It is a eukaryotic inhibitor isolated from Amanita phalloides which inhibits RNA II polymerase by blocking the initiation and elongation process.

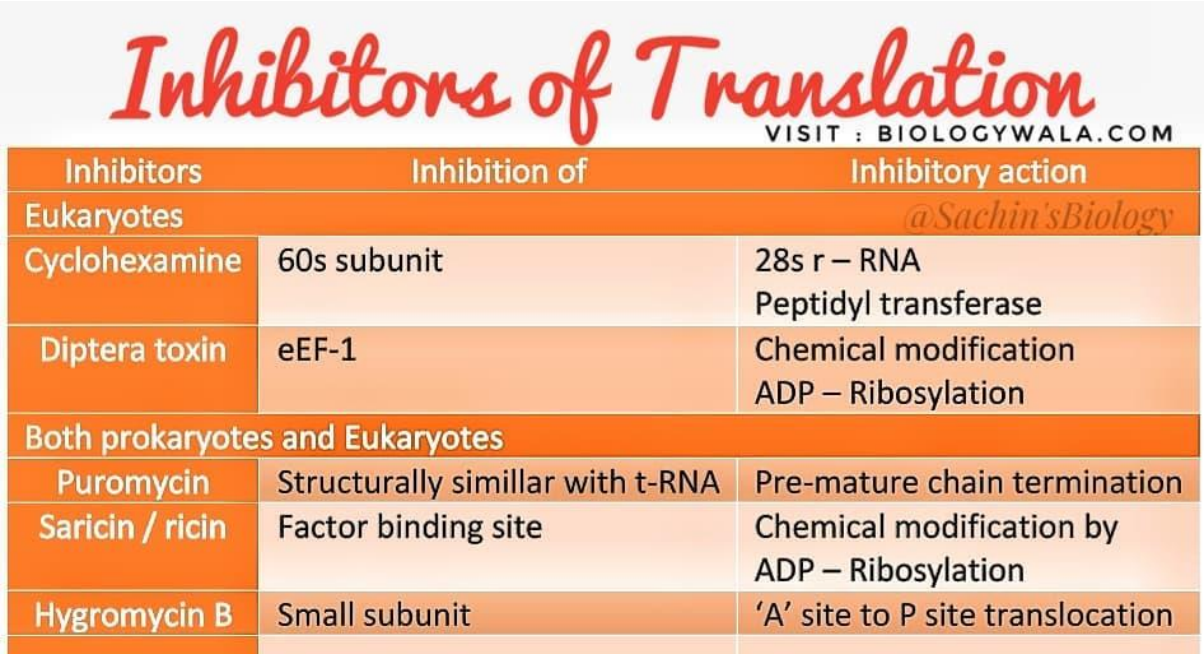
4. Cordycepin:

It shows the absence of hydroxyl moiety at the 3' position which inhibits transcription elongation and RNA synthesis.

5. Actinomycin D:

It is an antibiotic that shows antibacterial and antitumor activity. It inhibits the transcription of rRNA.

INHIBITORS OF TRANSLATION:



Inhibitors	Inhibition of	Inhibitory action
Eukaryotes		
Cyclohexamine	60s subunit	28s r – RNA Peptidyl transferase
Diptera toxin	eEF-1	Chemical modification ADP – Ribosylation
Both prokaryotes and Eukaryotes		
Puromycin	Structurally simillar with t-RNA	Pre-mature chain termination
Saricin / ricin	Factor binding site	Chemical modification by ADP – Ribosylation
Hygromycin B	Small subunit	'A' site to P site translocation

1.Streptomycin:

It blocks protein synthesis by binding to the 30S subunit and cause misreading of m-RNA which affects the initiation and leads to bacterial cell death.

2.Kanamycin, neomycin, gentamycin:

These are antibiotics that block initiation by binding to the 30S subunit of ribosomes.

3. Tetracycline :

Tetracyclines have activity against gram-positive and gram-negative bacteria. They prevent the growth of bacteria by inhibiting protein synthesis. It binds to the 30S subunit and interferes with aminoacyl -t-RNA binding. It also inhibits translocase by binding to the 50S subunit.

4. Azithromycins, Erythromycin, clarithromycin, dirithomycin :

Binds to 50S subunit and it blocks the protein synthesis by inhibiting transpeptidation.

5. Lincomycins:

In microbes, it binds to the 50S subunit and inhibits peptidyl transferase thereby inhibiting translation.

6. Puromycin:

It is an aminonucleoside antibiotic that inhibits protein synthesis by disrupting peptide transfer on ribosomes causing premature termination of protein synthesis by releasing peptidyl Puromycin.

7. Chloramphenicol:

It binds to the bacterial ribosomes and blocks peptidyl transferase thereby stopping bacterial growth, inhibiting protein synthesis.

8. Kirromycin:

It acts in elongation factor -Tu by interfering with the peptide transfer. It prevents the binding of aminoacyl t-RNA at the A site and so inhibits protein synthesis.

9. Fusidic acid:

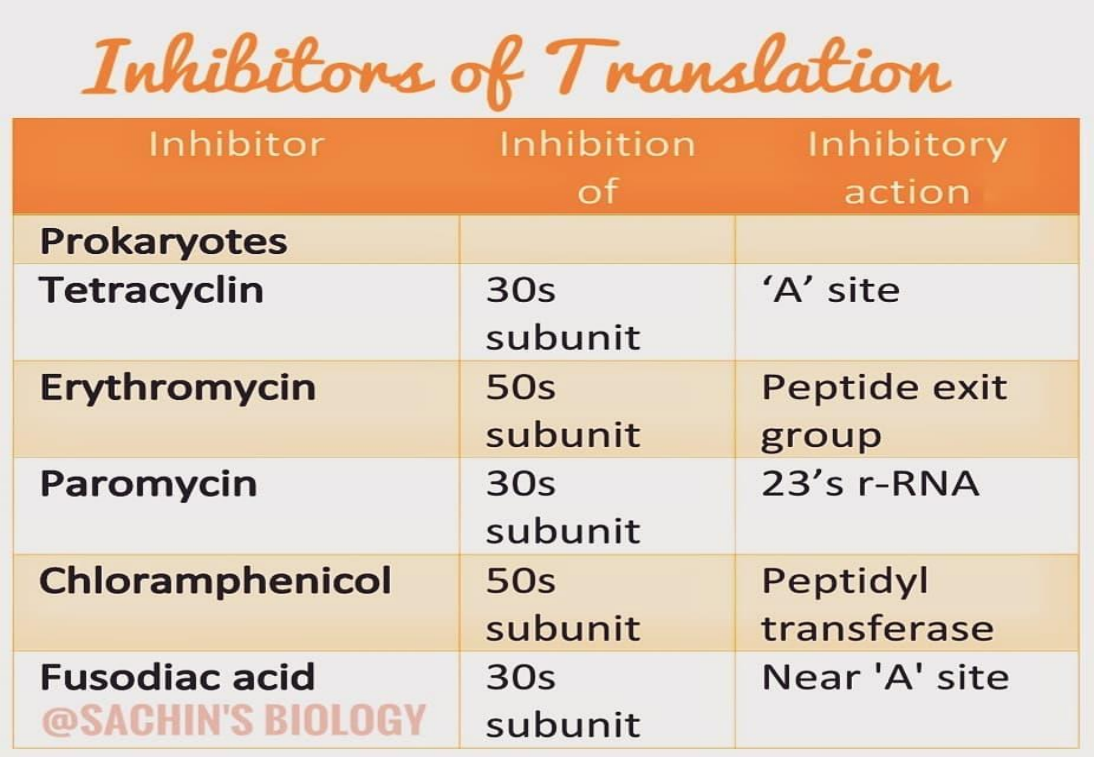
It binds to elongation factor- G-GDP which inhibits peptide translocation and so blocks protein synthesis.

10. Diptheria toxin :

Ef-2 is responsible for histidine residue modification which is inactivated by diphtheria toxin and protein synthesis is inhibited.

11. Ricin:

It is N-glycosidase that removes a single adenine base from one of the eukaryote ribosomal RNA and inactivates large subunits.



Inhibitors of Translation

Inhibitor	Inhibition of	Inhibitory action
Prokaryotes		
Tetracyclin	30s subunit	'A' site
Erythromycin	50s subunit	Peptide exit group
Paromycin	30s subunit	23's r-RNA
Chloramphenicol	50s subunit	Peptidyl transferase
Fusodiac acid	30s subunit	Near 'A' site

[PDF] Inhibitors of Transcription and Translation Notes 2

Here are some common questions related with Inhibitors of Transcription and Translation:

What are the inhibitors of transcription?

Ans-The Transcriptional Inhibitors, Actinomycin D and α-Amanitin Activate the HIV-1 Promoter and Favor Phosphorylation of the RNA Polymerase II C-terminal Domain* Actinomycin D and α-amanitin are commonly used to inhibit transcription.

2) What inhibits mRNA translation.

Silvestro inhibits the translation initiation by binding to the initiation factor eIF-4A which prevents the ribosome loading onto the mRNA template. This kills cells by inducing early autophagy and caspase-mediated apoptosis.

3) Which antibiotics inhibits translation in eukaryotes.

Cycloheximide inhibits peptidyl transferase activity in eukaryotes.