

SPT: 2.3A Molecular genetics

Lecture by

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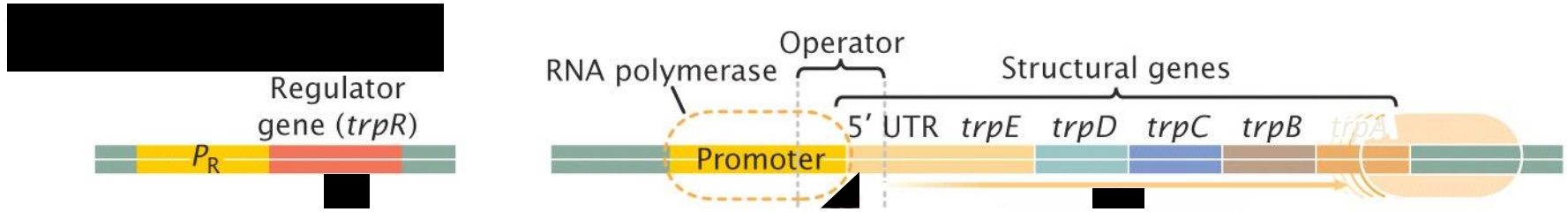
On

Unit – Gene Regulation

Regulation of the Trp Operon

- Repressible Operon
- Biosynthesis of Tryptophan
- Chorismate $\xrightarrow{\text{Enzymes}}$ Tryptophan
- Tryptophan level high ---- Co-repressor
- Co-repressor + Repressor ----- trp operon switched off
- Tryptophan level low ----- repressor inactive
- RNA polymerase @ Promoter region ---- trp operon switched on

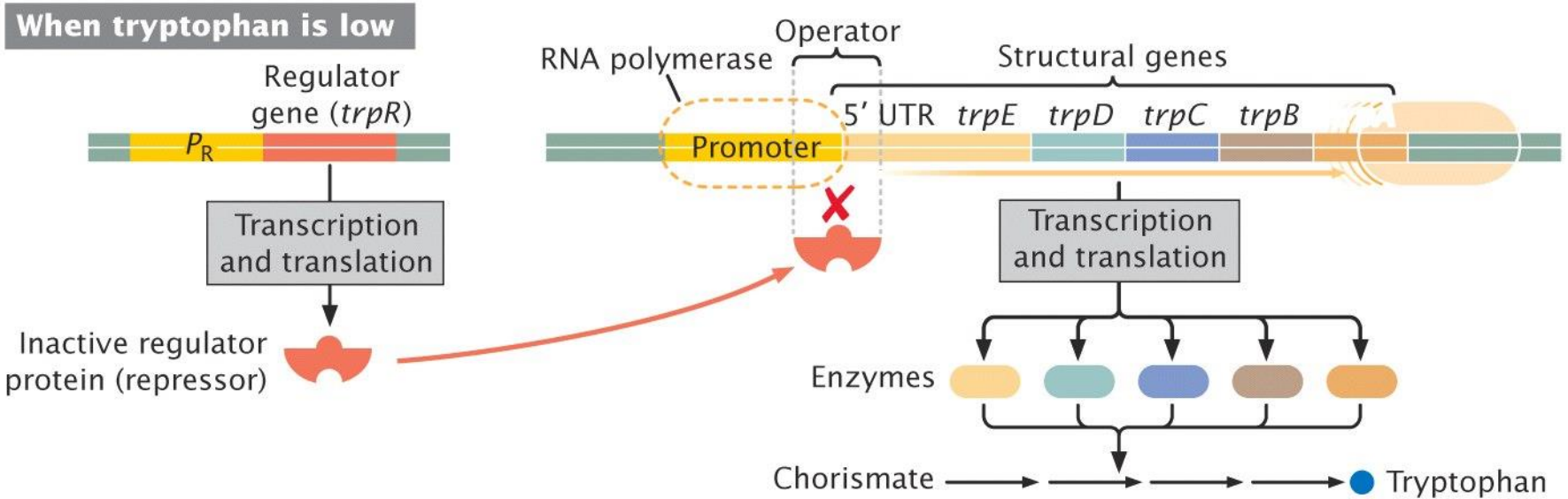
Tryptophan Operon



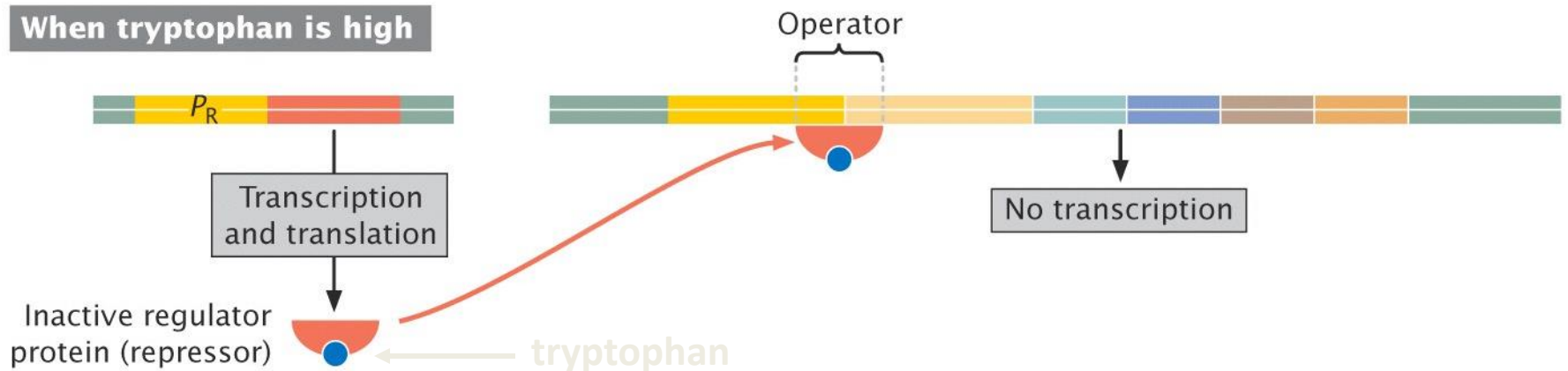
	DNA Function	RNA/Protein Function
Trp R	Gene for repressor	Binds to operator to inhibit transcription
P	Promoter	
O	Operator	
Trp E, D, C, B, A	Structural genes	Enzymes acting in pathway to produce tryptophan. Gene order correlates with order of reactions in pathway.
5' UTR (Leader)		Premature termination of transcription when trp levels are high

Control of Trp Operon Transcription

Trp Repressor is Inactive → Initial State: ON



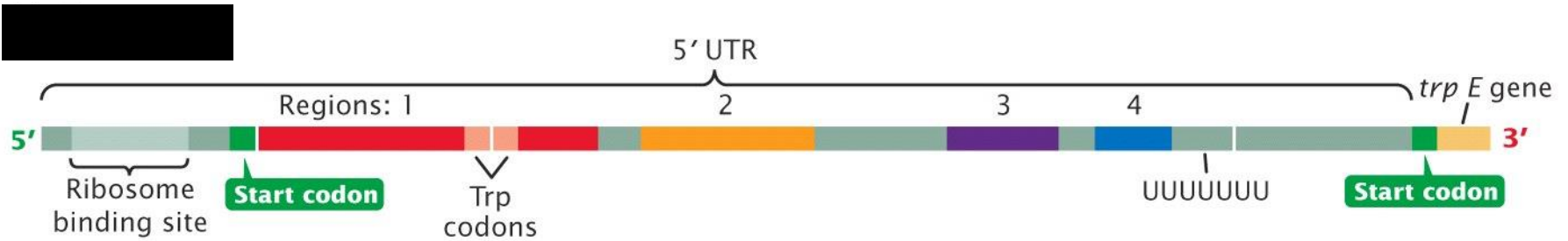
Trp binding activates Repressor → Final State: OFF



The Trp operon is also regulated by Attenuation

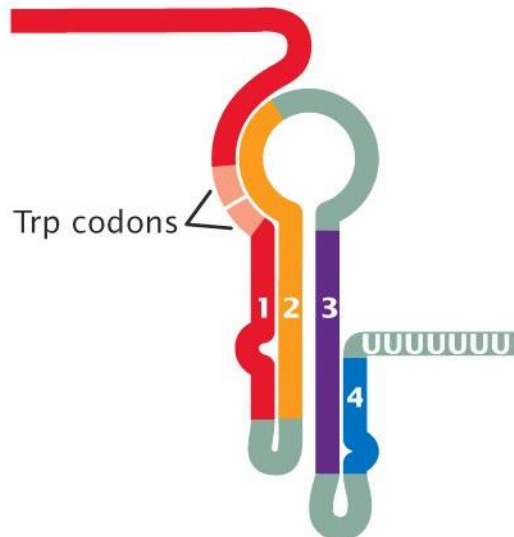
- An additional level of control that affects the continuation of transcription rather than its initiation .
- Premature termination of transcription process, before the RNAP even reaches the cistron.
- Occurs in no. operons--- biosynthesis of aminoacids.
- Charles Yanofsky et al., 1970--- **Attenuation**

Features of the 5' UTR

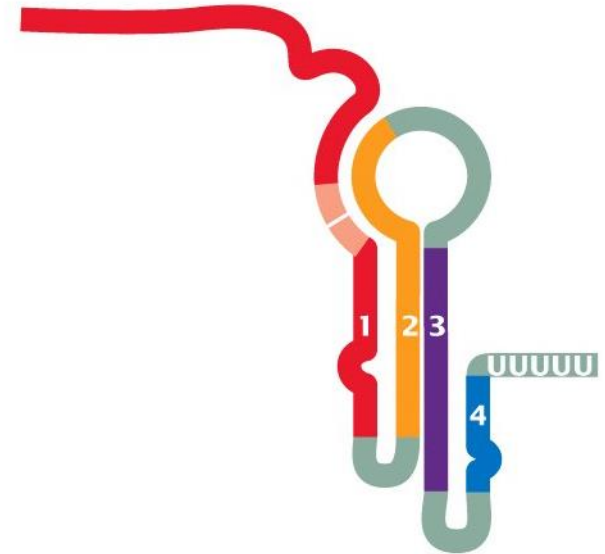


- Contains complementary sequences that can form hairpin structures when transcribed into RNA
- Codes for a stretch of U nucleotides that can act as a termination signal after a hairpin structure
- Codes for several Trp codons as part of an unstable protein product

Alternative RNA Structures from 5' UTR



1+2 and 3+4
secondary structure
Attenuation
(terminates transcription)



2+3
secondary structure
Antitermination

Termination signal due to hairpin formed by 3+4 pairing followed by string of uracils

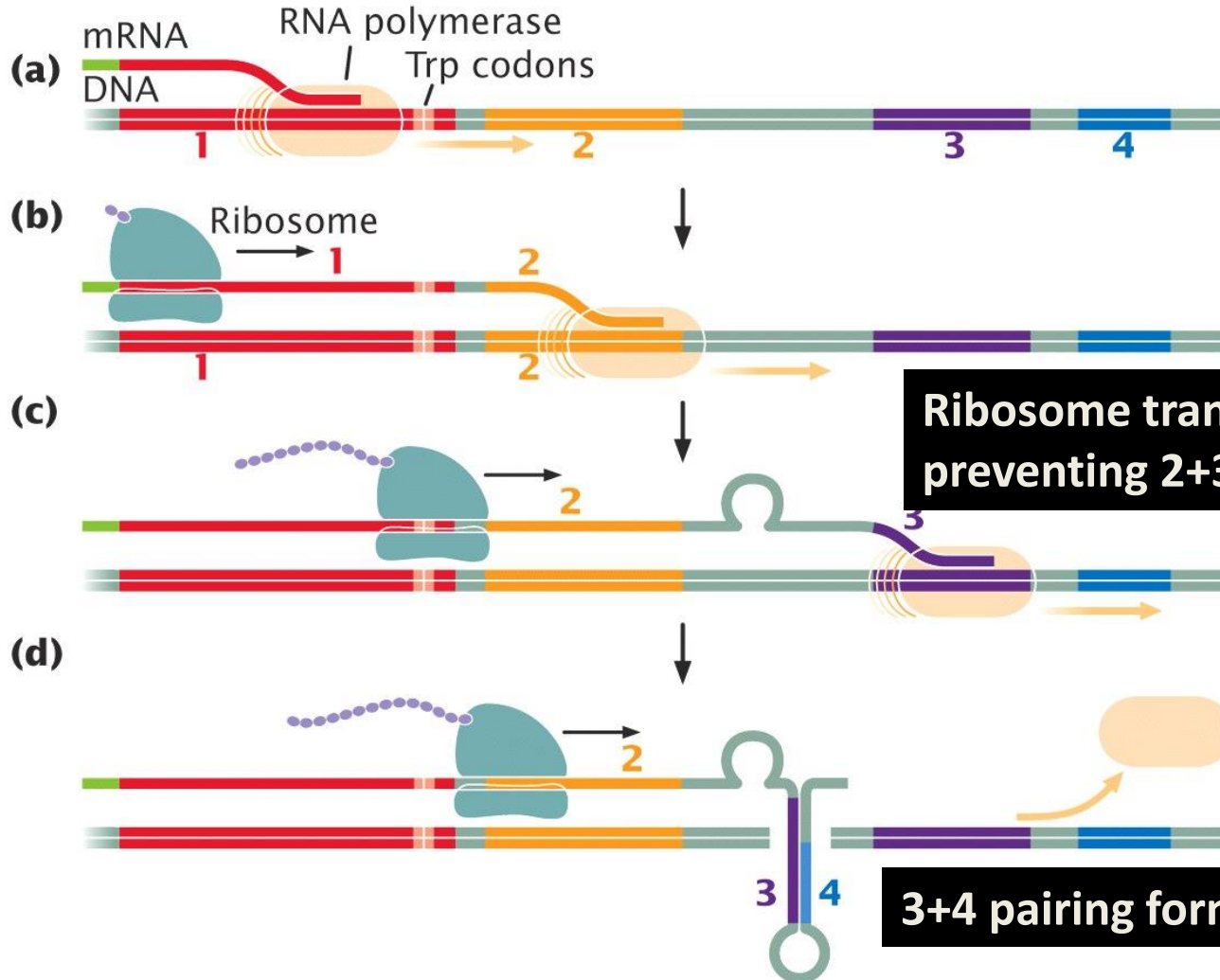
No termination signal formed

Formation of termination signal depends on level of tryptophan carried by tRNA in the cell.

Attenuation

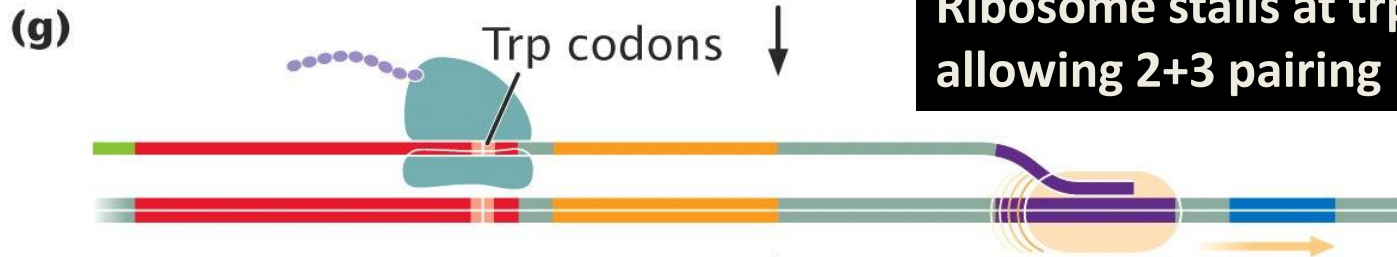
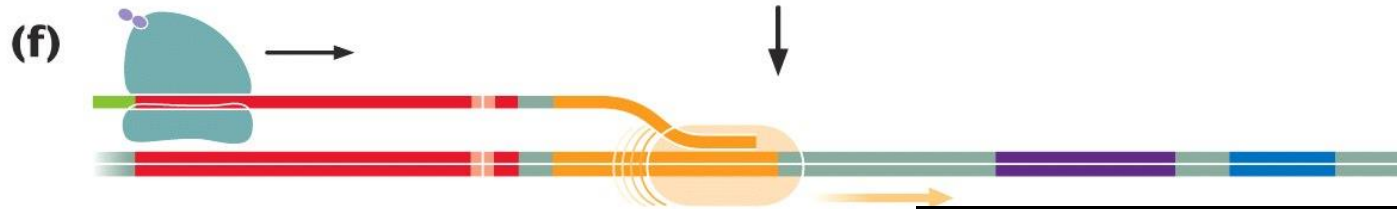
Premature Termination of Transcription

When tryptophan is high

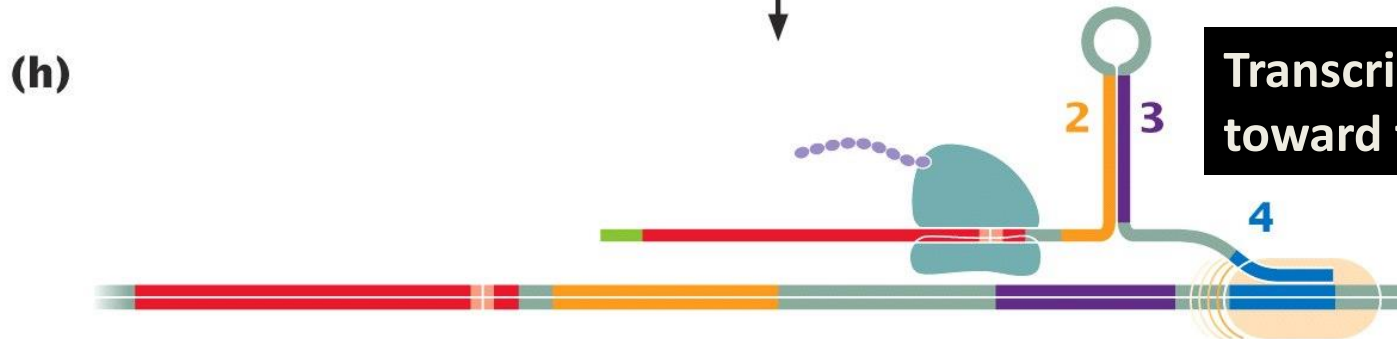


Antitermination

When tryptophan is low

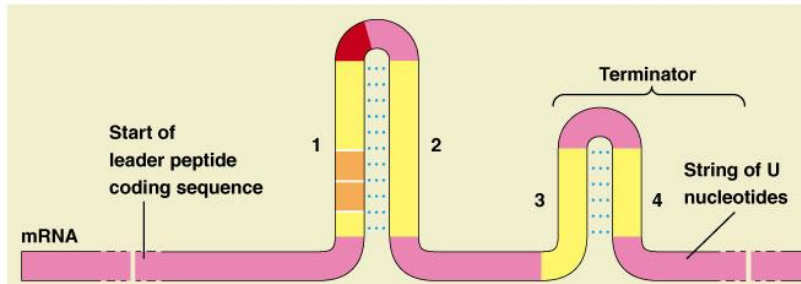


**Ribosome stalls at trp codons,
allowing 2+3 pairing**

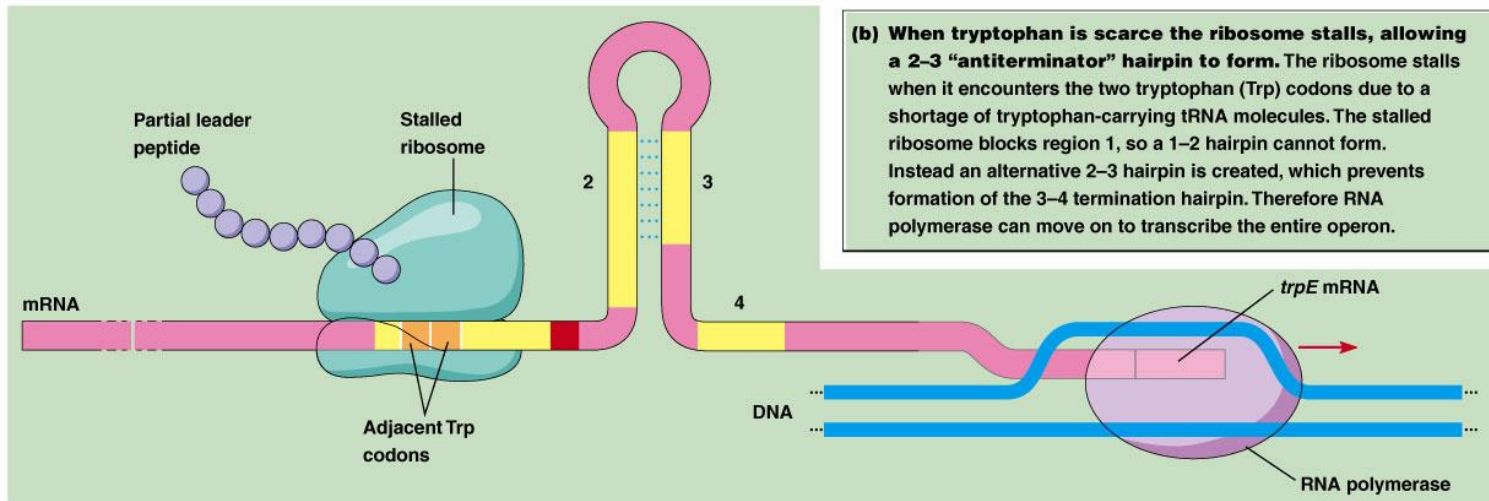


**Transcription continues
toward trp E, D, C, B, A**

Attenuation: The premature termination of transcription

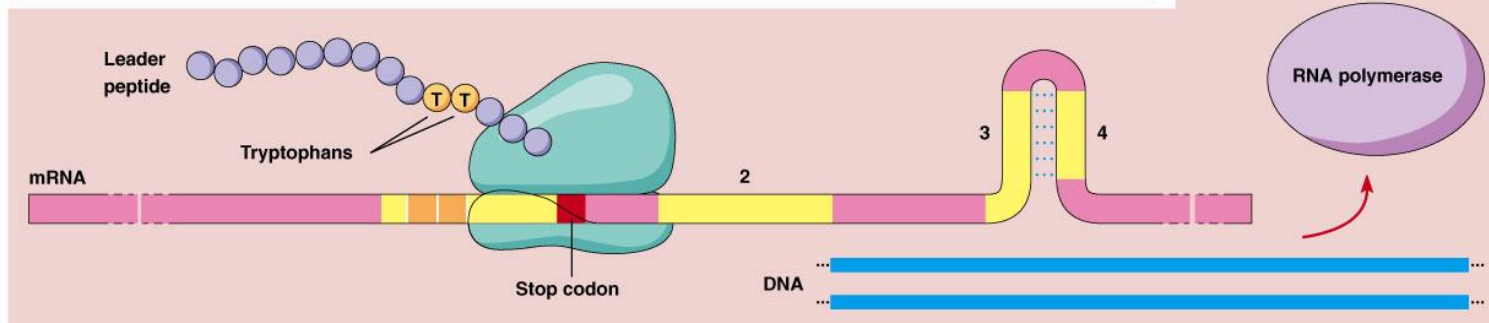


(a) The most stable secondary structure for *trp* leader mRNA. Attenuation depends on the ability of regions 1 and 2 and regions 3 and 4 of the *trp* leader sequence to base-pair, forming hairpin secondary structures. The 3-4 hairpin structure acts as a transcription termination signal.



(b) When tryptophan is scarce the ribosome stalls, allowing a 2-3 "antiterminator" hairpin to form. The ribosome stalls when it encounters the two tryptophan (Trp) codons due to a shortage of tryptophan-carrying tRNA molecules. The stalled ribosome blocks region 1, so a 1-2 hairpin cannot form. Instead an alternative 2-3 hairpin is created, which prevents formation of the 3-4 termination hairpin. Therefore RNA polymerase can move on to transcribe the entire operon.

(c) When tryptophan is plentiful the ribosome continues, allowing the 3-4 transcription termination signal to form. The moving ribosome completes translation of the leader peptide and pauses at the stop codon, blocking region 2. As a result, the 3-4 structure forms and terminates transcription near the end of the leader sequence.



Summary of Trp Operon Regulation

Level of Tryptophan	Trp Operon
Low	<p>On</p> <p>Trp repressor inactive Lack of attenuation leads to high rate of mRNA production</p>
High	<p>Off</p> <p>Tryptophan + repressor = Active repressor Reduction of mRNA production by attenuation</p>

References

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