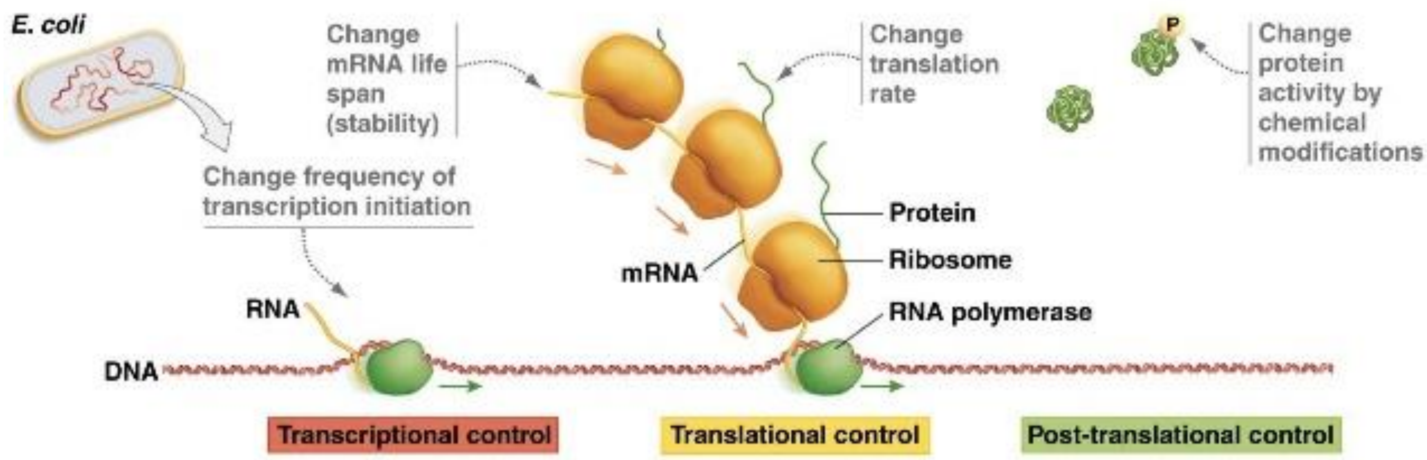
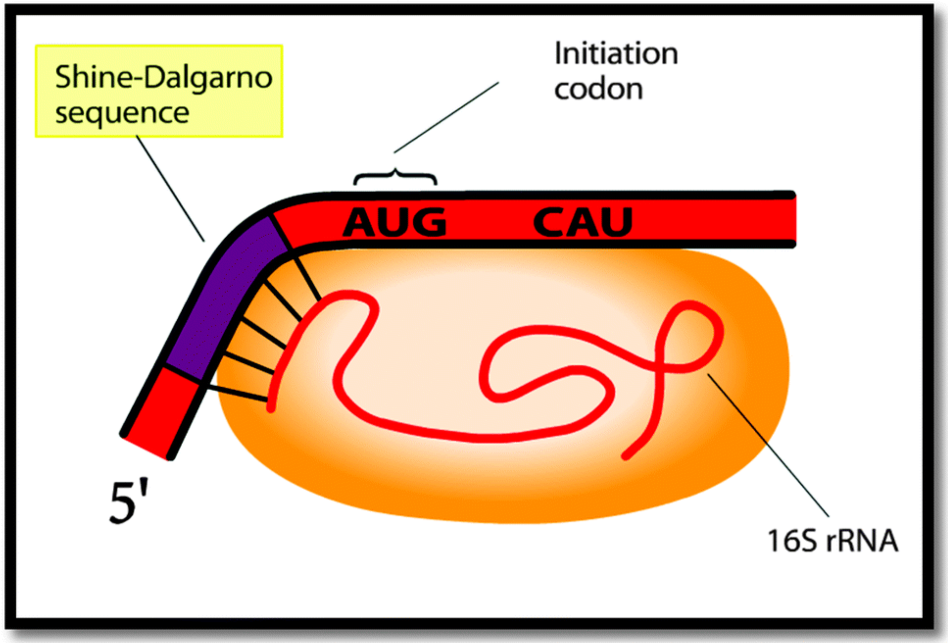
Regulation of Gene Expression

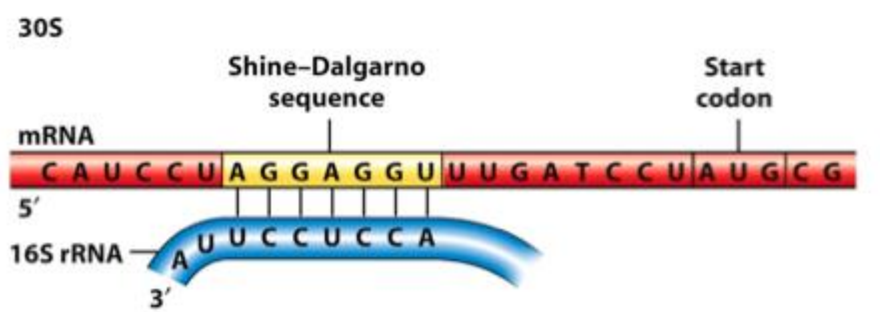


- Gene expression can be regulated:
  - During transcription (transcriptional control).
  - During translation (translational control).
  - After translation (post-translational control).

Translational control in prokaryotes

- In prokaryotes translation begins with binding of ribosome to a specific sequence in the messenger RNA - Shine-Dalgarno (SD) Sequence. SD is a ribosomal binding site generally located around 8 bases upstream of the start codon AUG. The six-base consensus sequence is AGGAGG. It is complementary to a specific region of 16S ribosomal RNA.


Shine-Dalgarno sequence
Initiation codon
AUG
CAU
5'
16S rRNA


30S
Shine–Dalgarno sequence
Start codon
mRNA
C A U C C U A G G A G G U U U G A T C C U A U G C G
5′
16S rRNA
A U U C C U C C A
3′

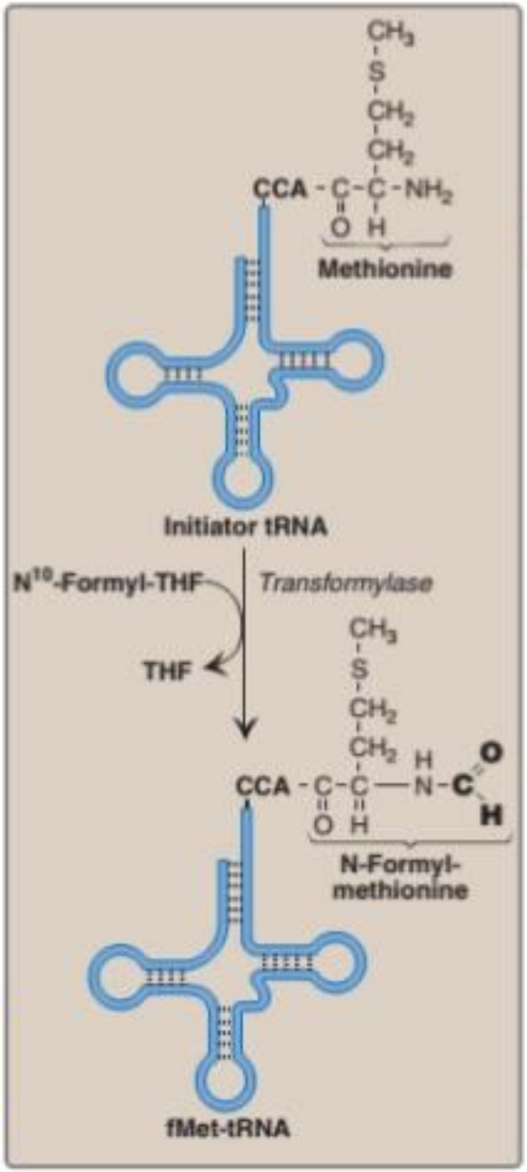
Initiation codon

- Initiating "AUG" is recognized by special initiator tRNA.

- Recognition is facilitated by **IF-2 (bound to GTP) in Prokaryotes** and **eIF2-GTP in Eukaryotes.**

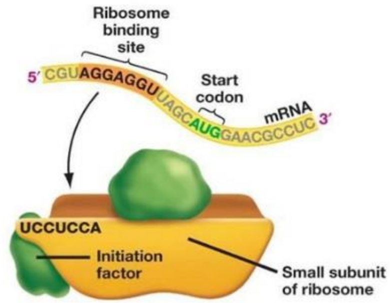
- The AA charged initiator tRNA enters the ribosomal P site, and GTP is hydrolysed to GDP.

NOTE: The initiator tRNA is the only tRNA recognized by eIF-2 and the only tRNA to go directly to the P site.



Translation initiation in bacteria

Shine-Dalgarno sequence

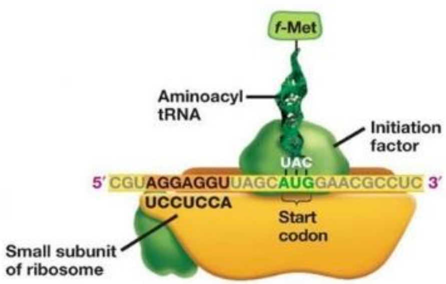


1. mRNA binds to small subunit of ribosome.

Translation initiation in bacteria

Initiator tRNA in bacteria

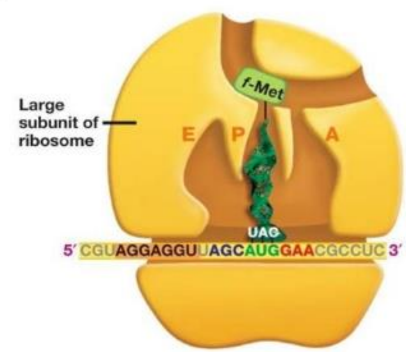
1.The initiator tRNA (fMet-tRNA) gets carried to the complex (30S ribosome + IF1 + IF 3) by initiation factor IF2 using GTP.



2. f-Met tRNA binds.

Translation initiation in bacteria

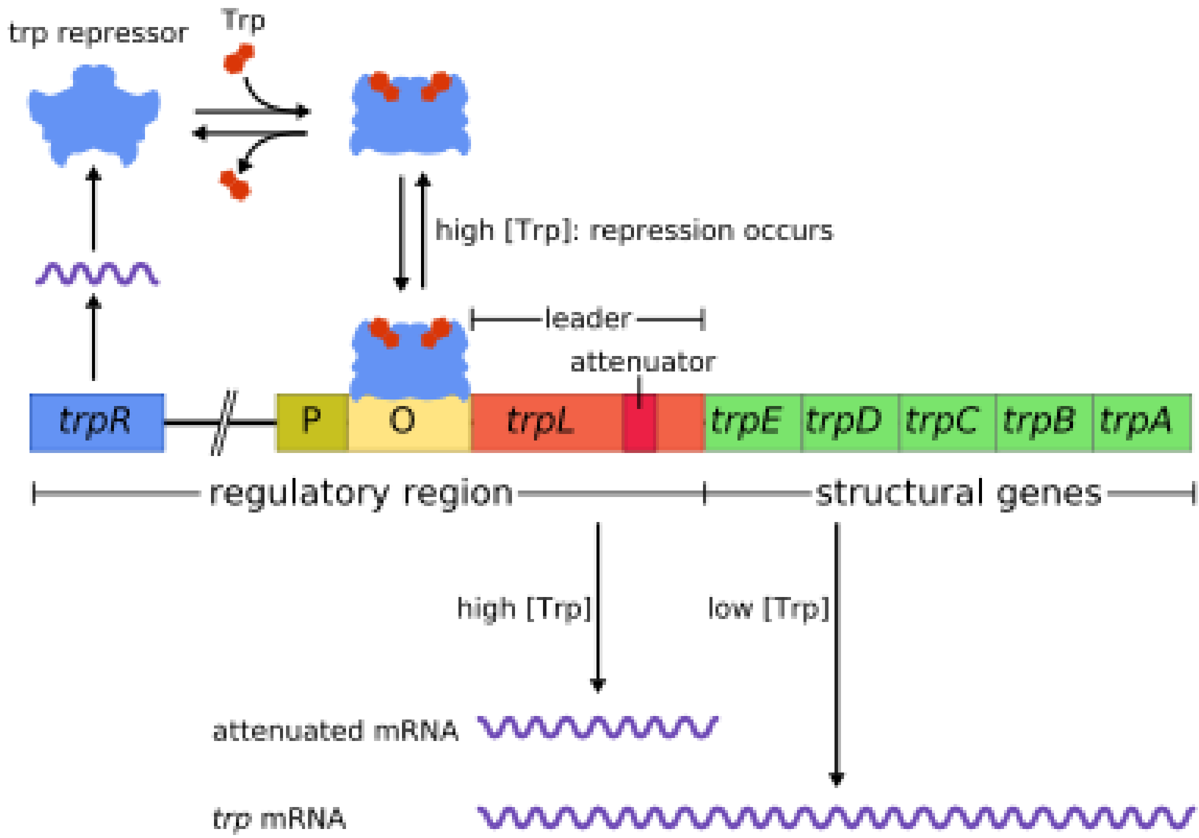
- The initiation factors (IF1 and IF3) gets released and the resulting complex is called **the initiation complex.**



3. Large subunit binds.

Attenuation of trp operon

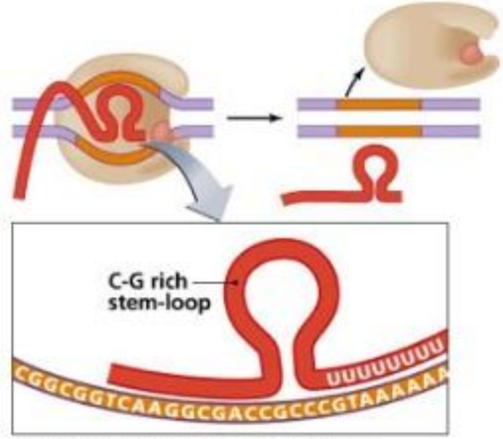
- Attenuation is a second mechanism of negative feedback in the trp operon. The repression system targets the intracellular trp concentration whereas the attenuation responds to the concentration of charged tRNAtrp
- Attenuation results in only 10% transcription rate of the trp operon structural genes
- Attenuation is made possible by the fact that **in prokaryotes** (which have no nucleus), **the ribosomes begin translating the mRNA while RNA polymerase is still transcribing the DNA sequence**. This allows the process of translation to affect transcription of the operon directly.


trp repressor
Trp
high [Trp]: repression occurs
leader
attenuator
trpR
P
O
trpL
trpE
trpD
trpC
trpB
trpA
regulatory region
structural genes
high [Trp]
low [Trp]
attenuated mRNA
trp mRNA

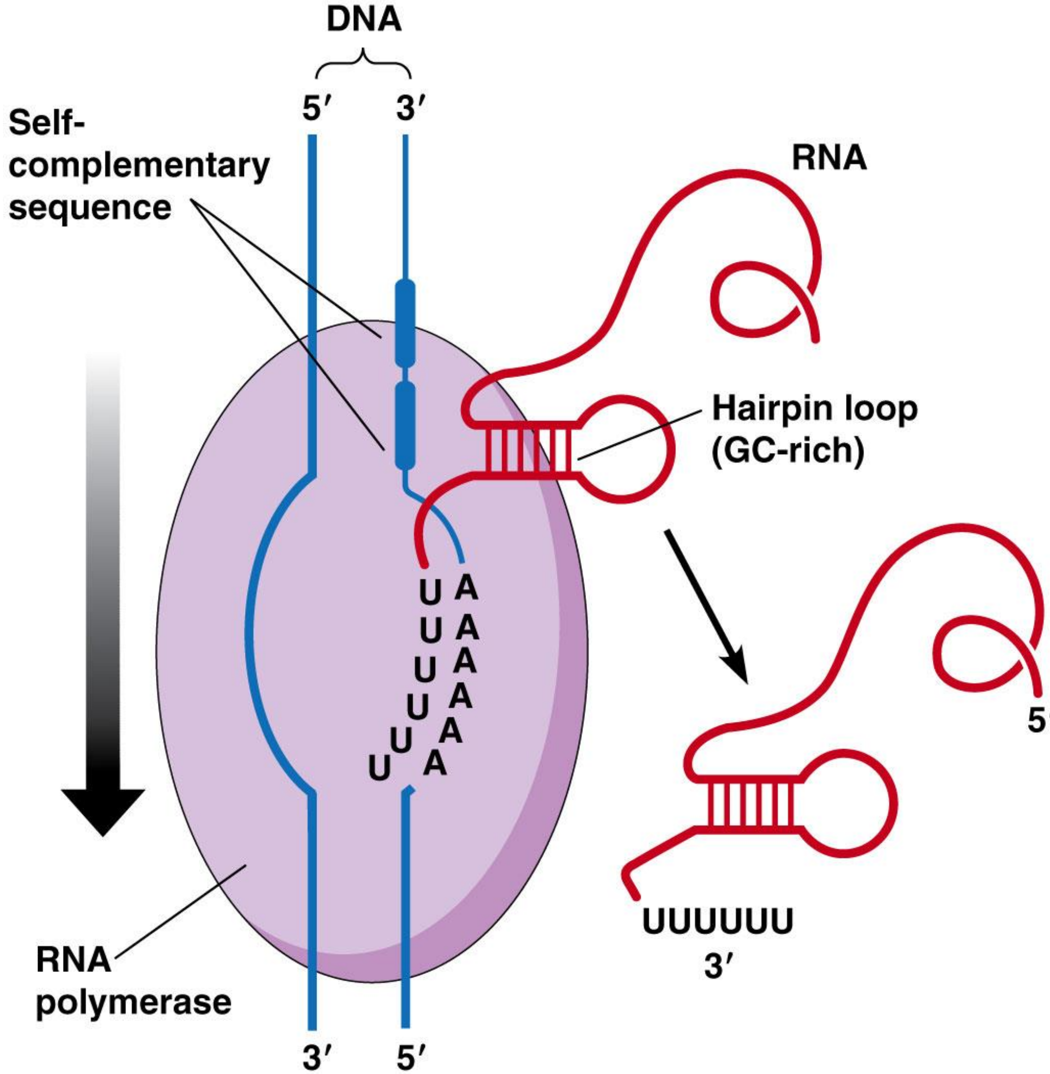
Bacterial transcription termination

Termination (Rho-independent terminator) - type 1 terminator

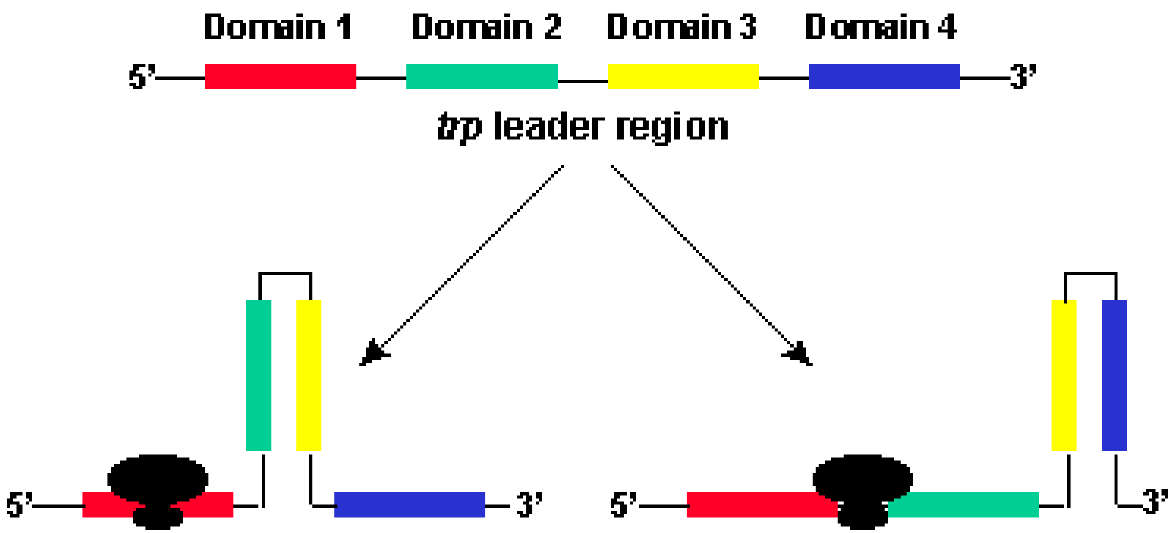
- RNA moves pass the inverted repeats and transcribes the termination sequence.
- Because of the inverted repeat arrangement ➔ RNA synthesized forms a hairpin loop structure.
- Hairpin loop makes the RNA polymerase slow down and eventually stops.



(c) Termination of transcription


DNA
5′
3′
Self-
complementary
sequence
RNA
Hairpin loop
(GC-rich)
U A
U A
U A
U A
U A
U A
5′
UUUUUU
3′
RNA
polymerase
3′
5′

Attenuation of the *trp* operon mRNA



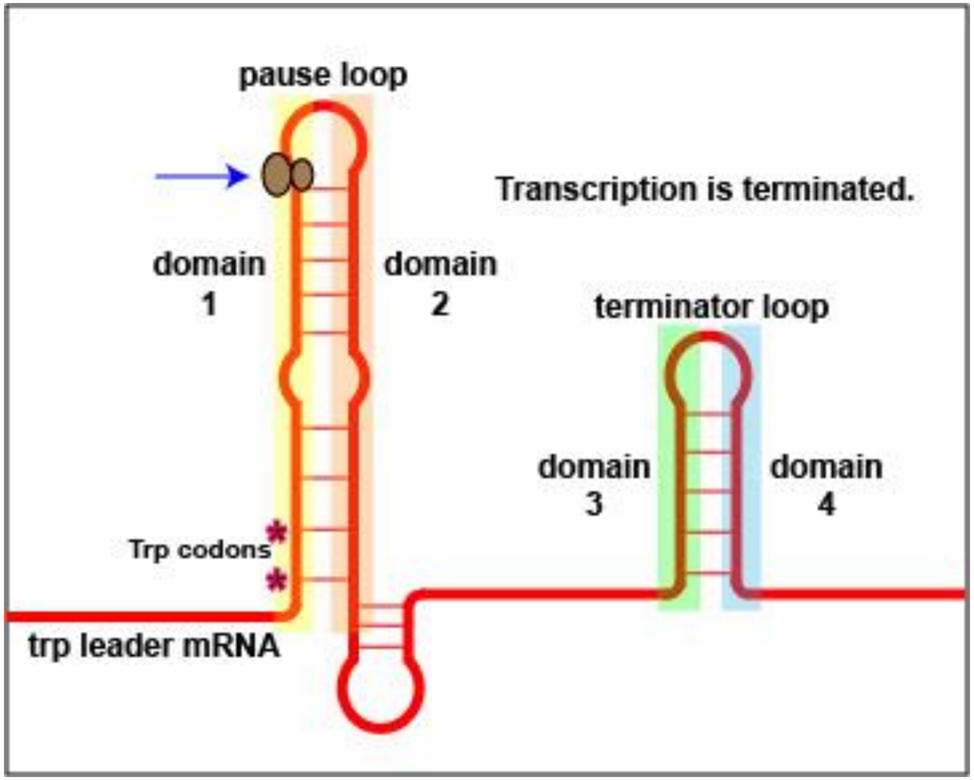
<u>Low Tryptophan Levels</u>

- Slow translation of Domain 1 peptide
- Domain 2-3 pairing occurs
- Normal full gene transcription

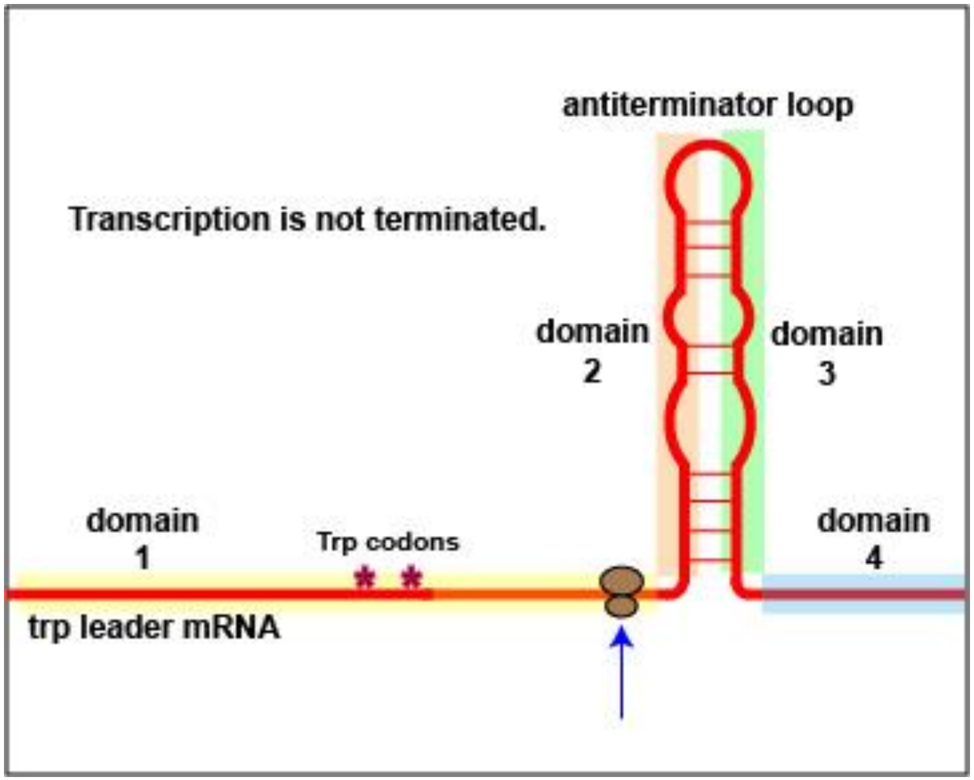
<u>High Tryptophan Levels</u>

- Fast translation of domain 1 peptide
- Domain 2 blocked by ribosome
- Domain 3-4 pairing occurs
- Attentuation of transcription occurs
- Only 10% of normal mRNAs made

Attenuation, tryptophan present



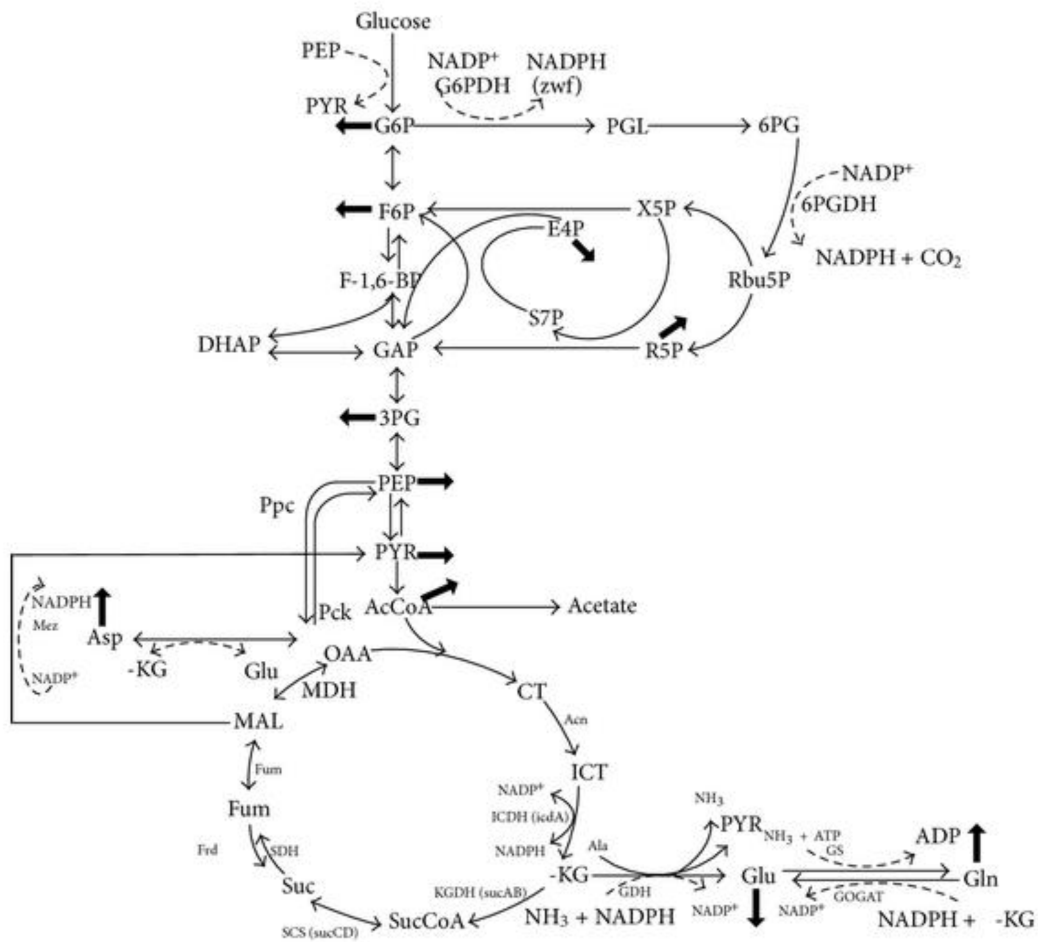
Attenuation, no tryptophan



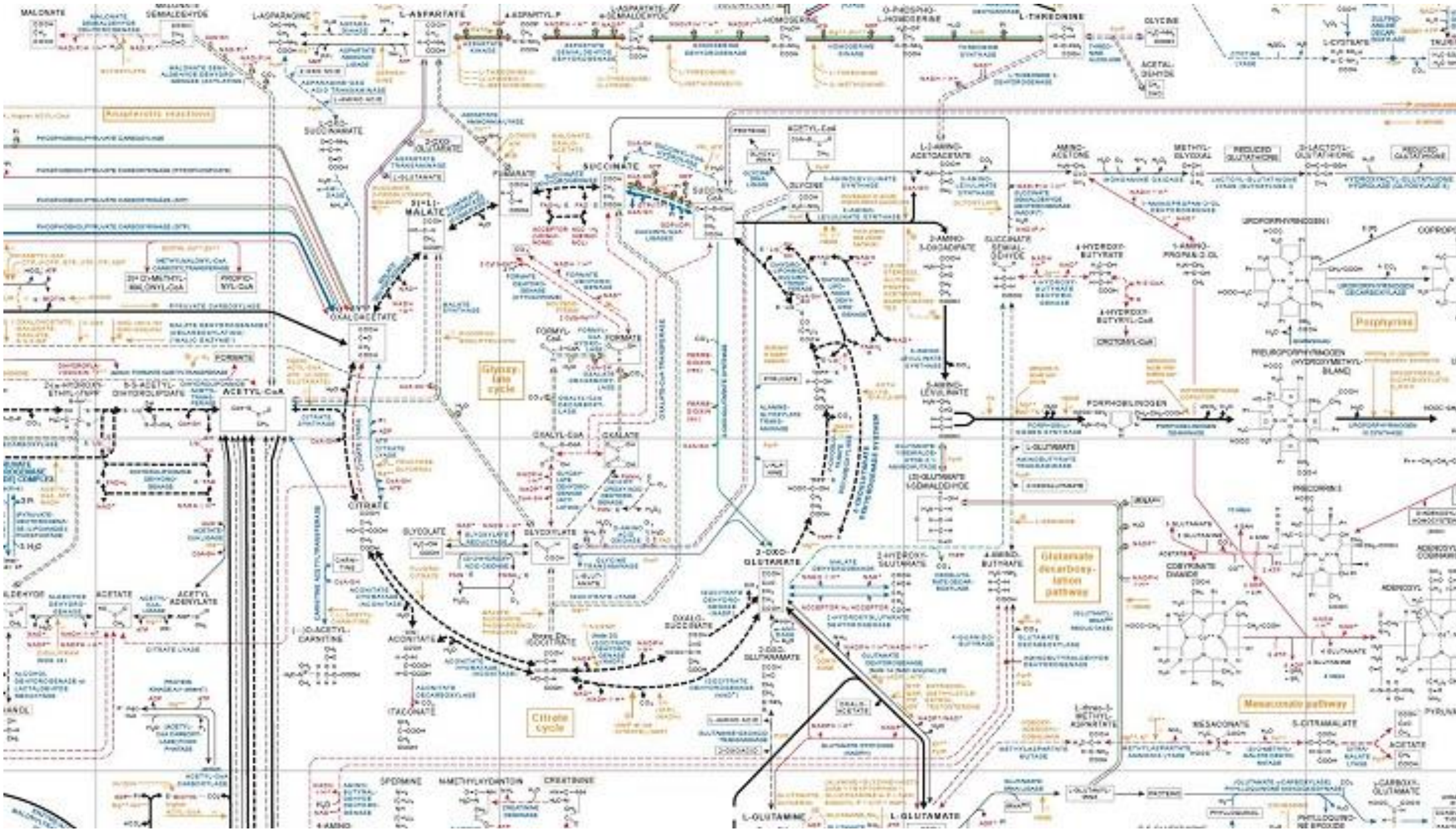
Biochemical Pathways

- A biochemical pathway (also called a metabolic pathway) is a series of enzyme-mediated reactions where the product of one reaction is used as the substrate in the next. Each enzymes is coded by a different gene.
- A network of complex interlocking mechanisms regulates expression of the enzymes.

Biochemical pathway of glucose catabolism in *E.coli*



Biochemical Pathways Chart



Unrelated fact

- The Perseverance rover landed on Mars last Tuesday. What is it looking for?

Strelley Pool Australian Archaean Stromatolites – 3.43 billion years old