Week 9
Genetics: BIO-2306

The concepts this resource covers are the topics typically covered during this week of the semester. If you do not see the topics your particular section of class is learning this week, please take a look at other weekly resources listed on our website for additional topics throughout the semester.

We also invite you to look at the group tutoring chart on our website to see if this course has a group tutoring session offered this semester.

If you have any questions about these study guides, group tutoring sessions, private 30 minute tutoring appointments, the Baylor Tutoring YouTube channel or any tutoring services we offer, please visit our website www.baylor.edu/tutoring or call our drop in center during open business hours. M-Th 9am-8pm on class days 254-710-4135.

Keywords: Ribosome, Amino Acids, Splicing, Codon, Polypeptides

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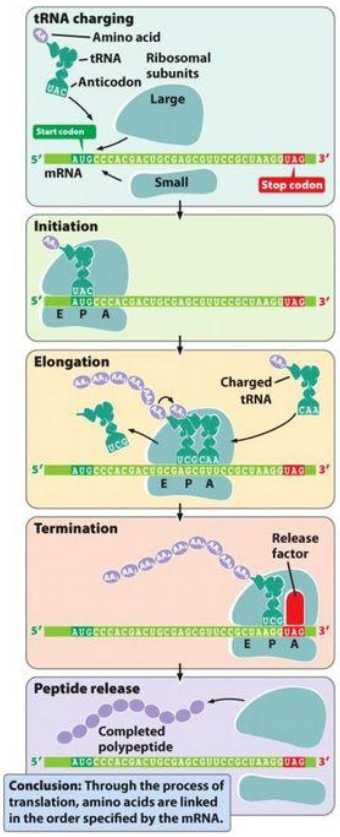
Topic of the Week: ***Translation*** (15.3)

Recall: the central dogma of molecular biology follows the flow of information from **DNA → RNA → Protein**



Translation: the synthesis of proteins from an mRNA code

Note: translation happens in the **5' → 3'** direction along an mRNA sequence; the polypeptide is synthesized in the $\mathbf{N}_{(amino)}$ terminus → $\mathbf{C}_{(Carboxyl)}$ terminus

Prokaryotic: simultaneous transcription and translation are possible, and use tRNA-*f-met* as initiator tRNA

Initiation: *IF-3* binds to small subunit (prevents complexing with large subunit); **Shine-Dalgarno** sequence on mRNA binds to small subunit at binding site; *IF-2* complexes with **GTP**, which binds to $tRNA_i^{f\text{-}met}$; *IF-1* binds to the small subunit as tRNA finds **AUG** codon and binding hydrolyzes **GTP** to GDP+P_i; all IFs leave; large subunit binds, forming 70s initiation complex.

Elongation: Ribosome has 3 sites*: **A**, **P**, and **E**

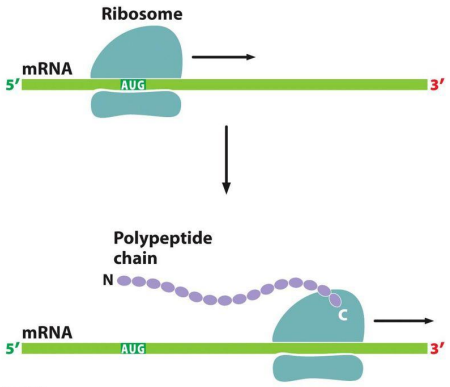
1. 70s complex has $tRNA_i^{f\text{-}met}$ occupying P-site
   a. *EF-Tu*-**GTP** and next charged tRNA form a complex; tRNA enters the A-site
2. **GTP** hydrolyzes to GDP+P_i and *EF-Tu* leaves

a. Peptide bond forms between the C-term of the AA in the P site and the N-term of the AA in the A site; *peptidyl transferase* activity of rRNA near p-site catalyzes this (elongate N → C)
b. The polypeptide chain transfers from P site to A site
   i. *EF-Ts* converts *EF-Tu*-GDP+P_i back to *EF-Tu*-**GTP**.

3. *EF-G* briefly associates with **GTP** to GDP+P_i hydrolysis, causing ribosome to *translocate* down the mRNA (in the 3' direction)
   a. tRNA with polypeptide chain moves to P-site
   b. tRNA *without* polypeptide is removed through the exit site

Termination: when a terminator (nonsense) codon is read in the A site:

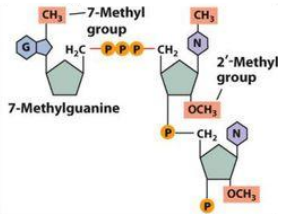
RF-1 or *2* binds to terminator codon in the A-site and *RF-3*-**GTP**.
Polypeptide chain at P-site is cleaved, and the chain is freed.
GTP to GDP+P_i hydrolysis releases RFs and dissociates ribosome-mRNA complex.



Eukaryotic:
https://www.youtube.com/watch?v=qIwrhUrvX-k

Initiation: $tRNA^i$ and eIF's bind to ribosome, then mRNA binds on the small subunit with help of ***CBPs***; large subunit complexes and hunts for **AUG**.
Elongation: *same process in eukaryotes as in prokaryotes*
Termination: *same process in eukaryotes as in prokaryotes*

Highlight #1: **pre-mRNA Processing** (14.2)

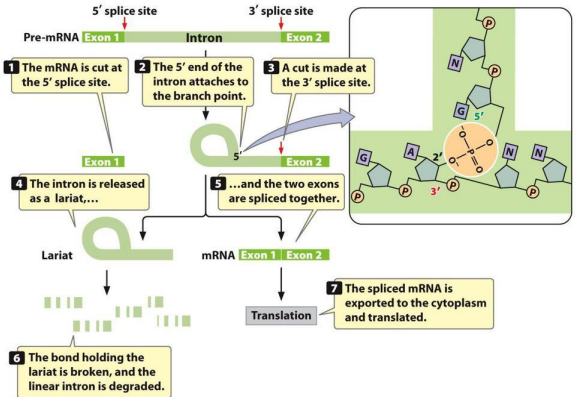


Spliceosomal Processing:

Addition of 5' Cap: 7-methylguanosine (modified guanine nucleotide) is added in a reverse 5'-5' bond to the polypeptide strand → prevents degradation and aids recognition of ribosome

3'-Cleavage and Polyadenylation: a consensus site (**AAUAA**) is recognized -11 to -30 bp from cleavage site; mRNA is cleaved between poly A and poly U consensus and a 50-250bp Adenosine (**poly-A**) tail is added to the 3' end of the cut → prevents degradation and stabilizes translation

Splicing: see diagram (***right***) snRNP = 1 snRNA + proteins → 5 snRNPs make up a ***spliceosome***



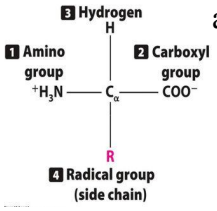
Alternative Processing: the same transcribed RNA molecule can be processed in multiple ways; thus, a single mRNA molecule can be *translated* into multiple proteins.

Alternate Splicing: different locations of splices and/or different rearrangement of exons

Multiple 3' Cleavage Sites: several different cleavage sites on the 3' end affects the position of polyadenylation

Note: *RNA processing* may occur in Euk's or Prok's, but **spliceosomal processing** will *only* occur in eukaryotes.

Highlight #2: **Codons and Wobble** (15.2)



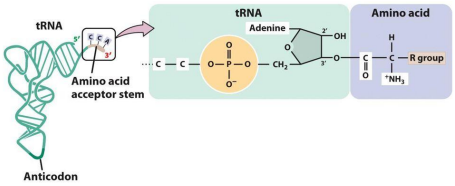
Codons: a sequence of 3 nucleotides on the mRNA (read 5' → 3') which code for a particular amino acid (***left***) → number of bases^3 = 4^3 = 64 codons ***(below right)***

Reading Frame: the non-overlapping sequence which a ribosome reads from the initiator (**AUG**) to a terminator

Sense Codons (61): more codons than amino acids, so some amino acids are coded by multiple *degenerate* codons

Initiator Codon (AUG): codes for *methionine* (Met) in eukaryotes and *n-formylmethionine* (f-met) in prokaryotes

Nonsense Codons (3): terminator codon (ie end translation) **UAA**, **UAG**, **UGA**.



tRNA Charging: energy requiring 2-step reaction where ***aminoacyl-tRNA synthetase*** adds an amino acid (**AA**) to the 5'-CCA-3' of the tRNA acceptor arm: AA + tRNA + ATP → aminoacyl-tRNA + AMP + $2P_i$

Second base

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

Wobble: flexible base pairing between the **3'** position of the codon and the **5'** of the anticodon.

5' C (anti) and **3'** G (codon)

5' G and 3' U or C

5' A and 3' U

5' U and 3' A or G

5' I and 3' A, U, or C

CHECK YOUR LEARNING

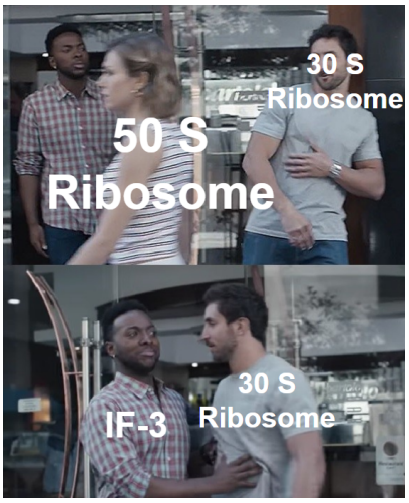
Concept Check: *(Answers found on last page)*

1. A tRNA has an anticodon **5'-I-U-G-3'**. Which of these mRNA could it **not** bind? *(multiple)*
   a. 5'-A-A-C-3'
   b. 5'-C-A-U-3'
   c. 5'-C-A-A-3'
   d. 5'-A-A-U-3'
2. What would not be expected to occur in eukaryotic cells?
   a. Polyadenylation of mRNA transcript

   b. Capping mRNA with a 5'-5' triphosphodiester-bound modified guanine
   c. Looping the 3'-splice site to form a bond to the 2'-OH of an Adenosine
   d. Joining exons and removing the intron lariat within the nucleus
3. The following RNA sequence would be translated to which amino acid sequence?
   5'-AUGAAAAUAGCAUACUGA-3' (hint: use **codon chart** from highlight 2)
   a. fMet-Lys-Leu-Gly-Cys-STOP
   b. Met-Lys-Ile-Ala-Tyr-STOP
   c. Lys-Lys-STOP
   d. Arg-Ile-Trp-Phe-Met-STOP
4. A cell is discovered and is kept alive while the researchers study it. The cell is roughly 8μm in diameter - too unambiguous to determine the cell type. If they look at a higher power and see polyribosomes, what type of cell will this be?
   a. Eukaryotic cell
   b. Prokaryotic cell
   c. Plant cell
   d. You can't tell because polyribosomes are native to many classes of cells
5. A particular drug binds to and inhibits the recognition site of *IF-2*'s tRNA binding site. What would be the *primary* effect of this?
   a. Spliceosomes would not cleave the 5' splice-site of pre-mRNA
   b. The DNA code would not match the translated protein's codons
   c. The Shine-Dalgarno sequence would not bind to the small subunit
   d. $tRNA^i$ would not bind to the **AUG** codon on the small subunit
6. A particular drug binds to and inhibits the recognition site of *IF-2*'s tRNA binding site. What does it likely do on a broad scale?
   a. Inhibit plant-cell replication
   b. Inhibit viral replication in animal cells
   c. Inhibit bacterial infection without affecting eukaryotic translation
   d. Preventing tumor formation by inhibiting target gene transcription
7. What does the 5' splice site bind to form the lariat?
   a. Adenosine Residue (2'-OH)
   b. Guanine Residue (2'-OH)
   c. Cytosine Residue (3'-OH)
   d. Adenosine Residue (5'-OH)
8. What is <u>not</u> an immediate result of *EF-Tu* bound **GTP** hydrolysis?
   a. *EF-Tu* dissociates from ribosome
   b. Peptide bond is formed between the A site and P site
   c. Polypeptide chain is transferred to the tRNA in the A site
   d. Ribosome slides in the 3' direction down the mRNA

THINGS YOU MAY STRUGGLE WITH:

1. Terminology: "IF" = initiation factor; "eIF" = eukaryotic; "EF" = elongation factor; "RF" = release factors; "AA" amino acids; *"**A [site]**" = aminoacyl site; "**P**" peptidyl site; "**E**" exit site; "CBP" = cap-binding proteins; "N-term" = N-terminus ($-NH_3^+$); "C-term" = C-terminus ($-COO^-$)
2. Eukaryotic cells do <u>not</u> have a Shine-Dalgarno sequence; CBPs help complex mRNA with ribosome (bound to $tRNA^i$) and the small subunit "scans" until it finds the **AUG** codon on mRNA
3. Polyribosomes are single mRNA molecules simultaneously *translated* by multiple ribosomes used by both prokaryotes <u>and</u> eukaryotes to increase the efficiency of translation
4. Hydrolyzing **GTP → GDP + P_i** causes things to leave or dissociate, or gives energy for movement/bonding
5. Release factors <u>don't</u> have AA's bound, but ***<u>do</u>*** have anticodons.



CONGRATS: You made it to the end of the resource! Thanks for checking out these weekly resources! Don't forget to check out our website for group tutoring times, video tutorials and lots of other resources: www.baylor.edu/tutoring!

Answers to check your learning questions are below!

Answers:

1. A, D
2. C
3. B
4. D
5. D
6. A
7. D
8. D