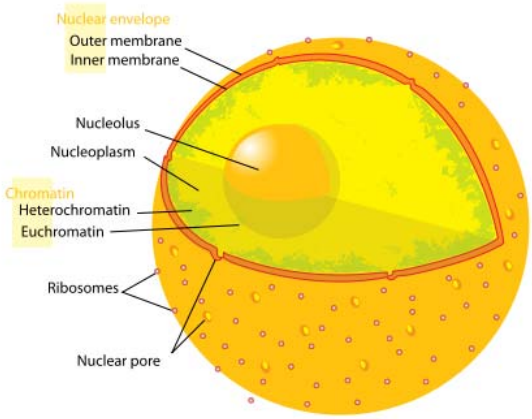
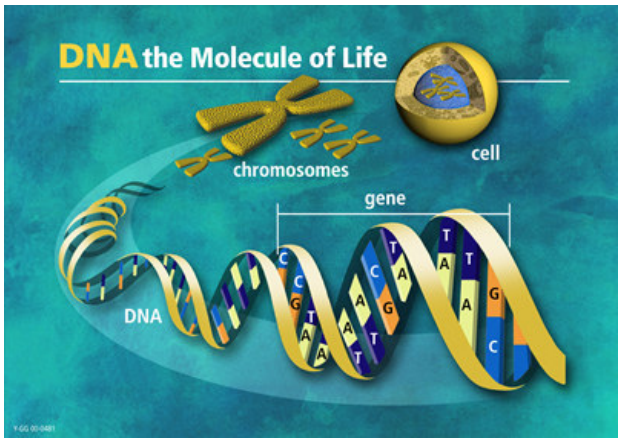
From Gene to Protein Notes
AP Biology Mrs. Laux

Nucleus is control center of the cell



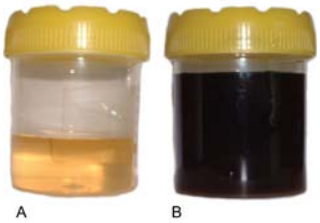
-DNA/chromosomes control all of the activities of the cell and yet are never directly involved in the activities.



-Rather, each gene that encodes for a "trait," actually is a template for an enzyme (or other protein) that will cause that trait to be expressed.
-Remember that genes carry a template for protein→can be modified into enzyme
    -no reactions occur if there is no enzyme present
    -reactions will occur if an enzyme is present
-Therefore, by making enzymes (or not), the nucleus determines whether or not a certain trait will be carried out

DNA→Gene→Protein→Enzyme→Expression of Trait

1909-Archibald Garrod
    -studied people with alkaptonuria (black urine)



-through studies, he concluded that people lacked protein (enzyme) that breaks down alkapton
-this was a disease that was genetic in nature (passed on from parent to offspring)
-because lacked enzyme, obviously genetic, he reasoned that there was a problem with a particular gene
-he was one of the first to propose that genes dictate phenotypes through enzymes that catalyze reactions

-Garrod's hypothesis was confirmed several decades later

Beadle and Tatum 

-demonstrated relationship between genes and enzymes by studying mutants of bread mold, *Neurospora crassa*
    -can survive on minimal medium
    -all other molecules are produced by its own metabolic pathways from medium (salts, sucrose, vitamin biotin)
-auxotrophs-cannot survive on the minimal medium
    -lacked ability to synthesize certain molecules
    -need complete growth medium
        -all 20 amino acids and some other nutrients

-Beadle and Tatum identified metabolic defects (mutations) in mutants, by growing auxotrophs in mediums supplemented with only one additional nutrient
-vial where growth occurred-the single supplement provided necessary component
-ex: if mutant grew on medium and arginine-shows that mutant was unable to synthesize arginine; therefore, lacked enzyme needed to synthesize arginine
-found that different classes of mutants were unable to synthesize arginine at varying points in the pathway
-concluded that they lacked enzymes to do this

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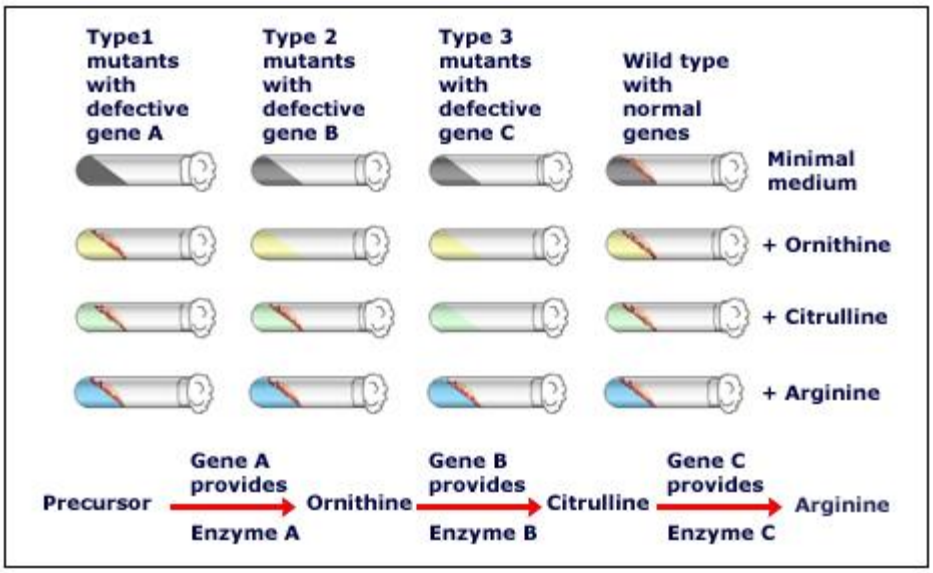
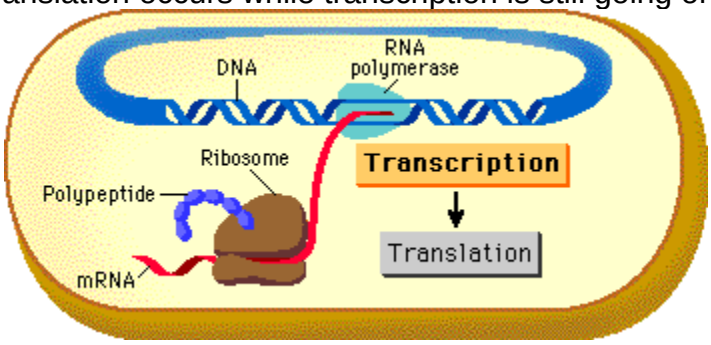


-assumed that each mutant was defective in a single gene-and formulated **one gene-one enzyme hypothesis**
-function of a gene is to dictate production of a particular enzyme

-Today-modified-one gene-one polypeptide (or one nucleic acid) hypothesis
1. many proteins are not enzymes
2. many enzymes contain more than one polypeptide (4^o)

Protein synthesis
-template for protein is contained in DNA (gene)
-involves the process by which the message in DNA is transcribed into blueprint (mRNA) and translated into the amino acid sequence
-differs between prokaryotes and eukaryotes
-Prokaryotes-lack nuclei-DNA is not segregated from ribosomes; therefore, translation and transcription occur in rapid succession
-translation occurs while transcription is still going on



-Eukaryotes-nuclear envelope→transcription→nucleus translation→cytoplasm; therefore, process of RNA processing that occurs in eukaryotes

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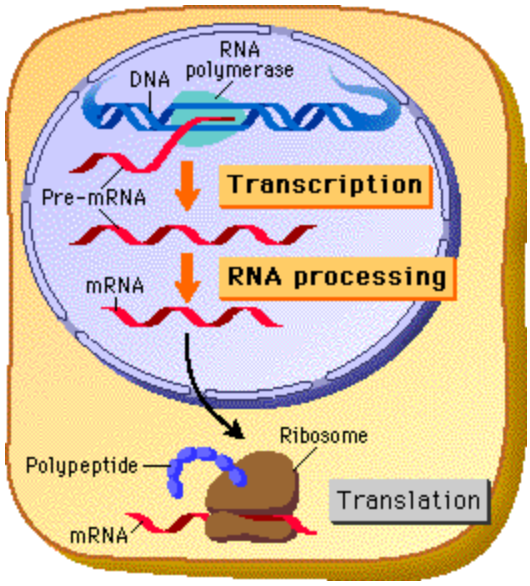

DNA
-every adjacent 3 nucleotides in DNA encode for a certain amino acid
-in RNA-copy of these 3 nucleotides is a codon (or triplet codon)
-with 4 nucleotides-64 possible codons
-20 amino acids
-therefore, several codons encode for a given amino acid

Second letter

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

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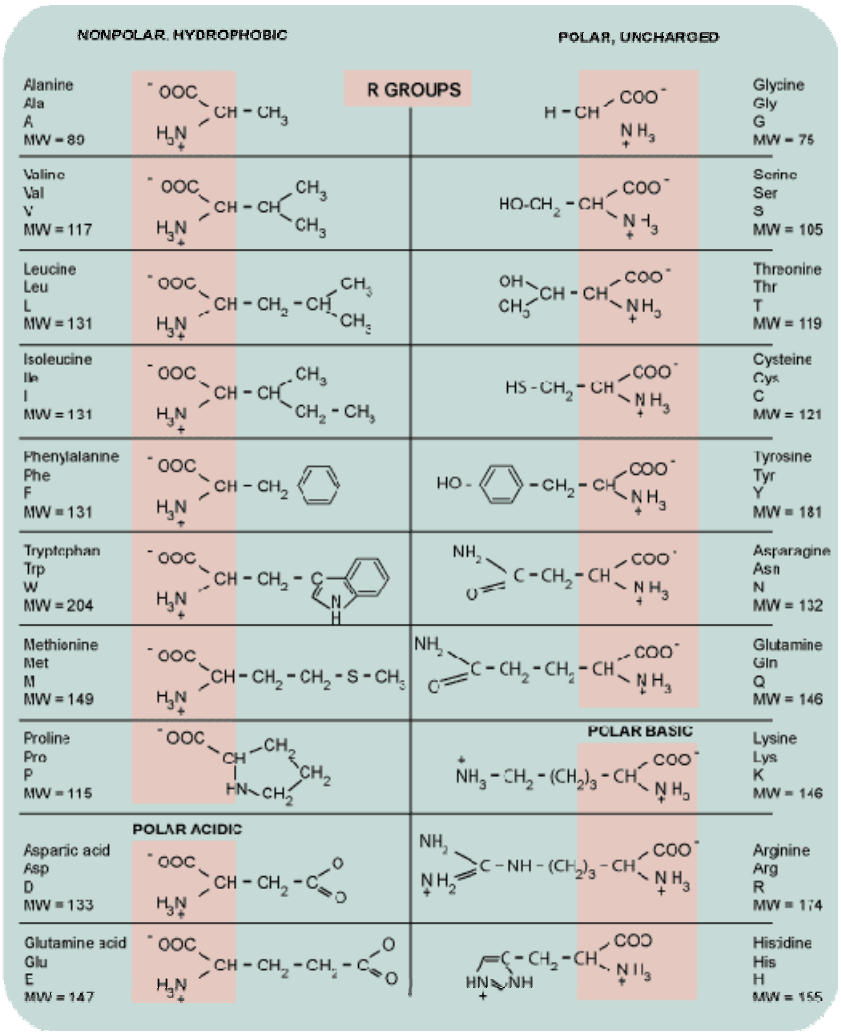
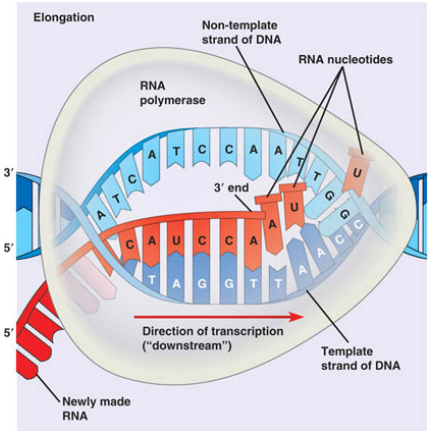


3 Stages of Synthesis

I. Transcription

-copying of DNA template strand (sense strand)→runs in 3'→5' orientation
-just like in DNA replication, nucleotides can only be added on the 3' end
-therefore, mRNA strand grows 5'→3'
-creates codons



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3 Types of RNA

1. mRNA → single strand of RNA that provides template for the sequencing of amino acid into a polypeptide

-codons:

-ex: CGA→arginine

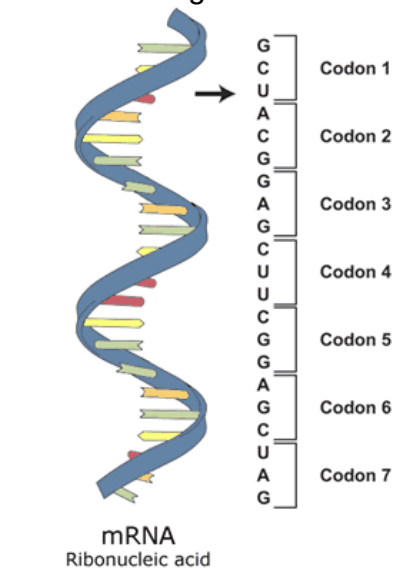


Image adapted from: National Human Genome Research Institute. Talking Glossary of Genetic Terms. Available at: www.genome.gov/Pages/Hyperion/DIR//VIP/Glossary/Illustration/codon.shtml.

2. tRNA → short RNA molecule

-~75-80 nucleotides

-transports amino acids to their proper place on the polypeptide

-sequence of nucleotides results in base-pairing between nucleotides

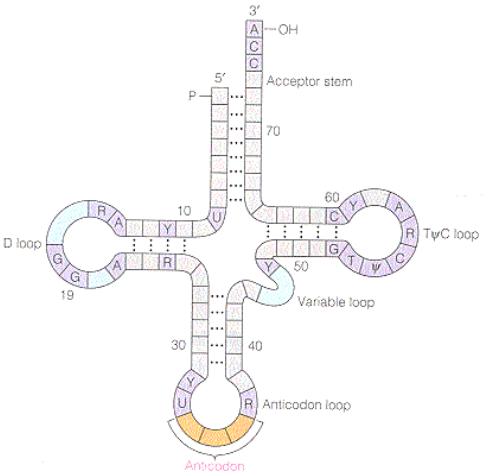
-folds-3-D shape-3 leaf clover

-3' end of tRNA-ends with C-C-A

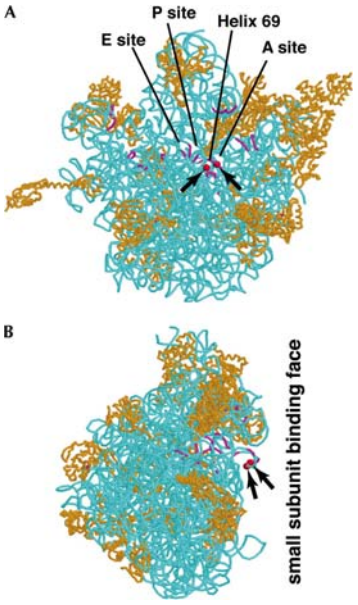
-where specific amino acid attaches

-bottom of clover-contains the anticodon

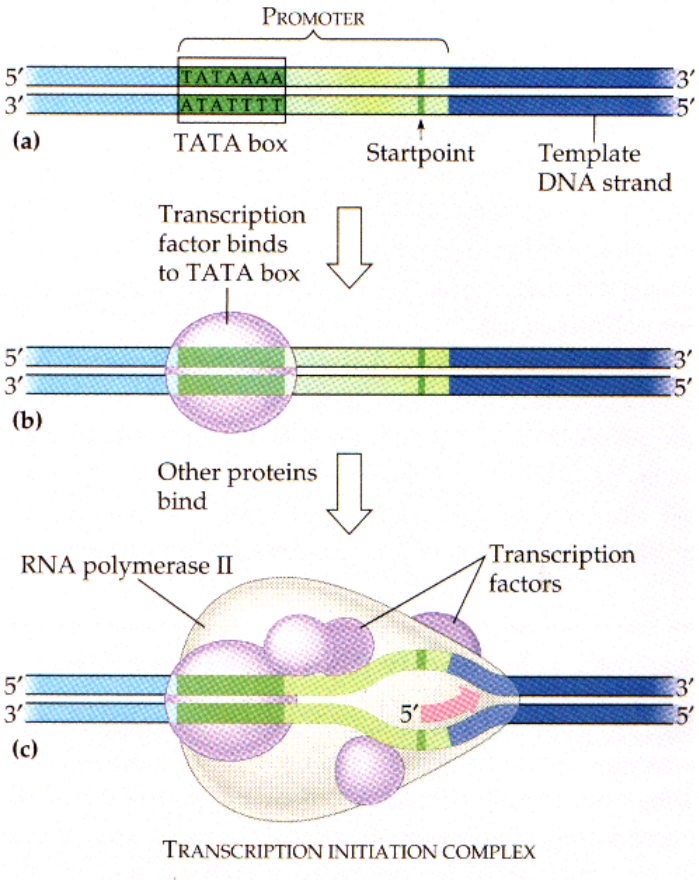
-anticodon pairs with codon on mRNA-transferring the specific amino aicd that the codon calls for



3. rRNA → building blocks of ribosomes
-ribosomes are organelles that are synthesized in the nucleolus
-contain 50 to 60% rRNA and 40 to 50% proteins
-2 parts→large and small subunits
-2 come together in cytoplasm during protein synthesis to form a ribosome

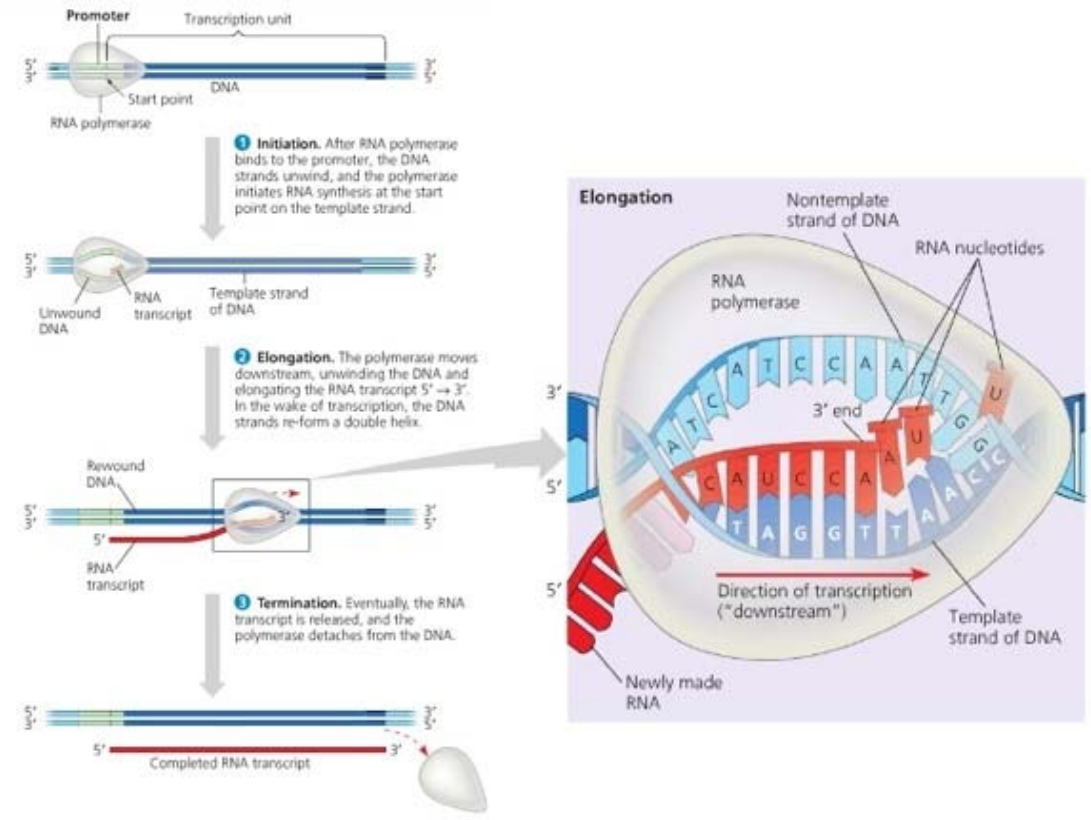


I.Transcription (cont.)
A. Initiation
-RNA polymerase
-separates 2 strands of DNA
-builds mRNA as complimentary to DNA sense strand
-builds 5'→3'
-binds at promoter region of DNA and unzips DNA
-begins transcription
-initiation site→ ~100 nucleotides long
-contains sequence T-A-T-A called TATA box
-transcription factors help RNA polymerase recognize the promoter
-DNA-binding proteins



B. Elongation
- -nucleotides are added at the 3' end
- -RNA nucleotides, not DNA

C. Termination
- -continues until RNA polymerase reaches a termination site in DNA
- -signals a stop of transcription
- -most common→in eukaryotes→AAAAAAA

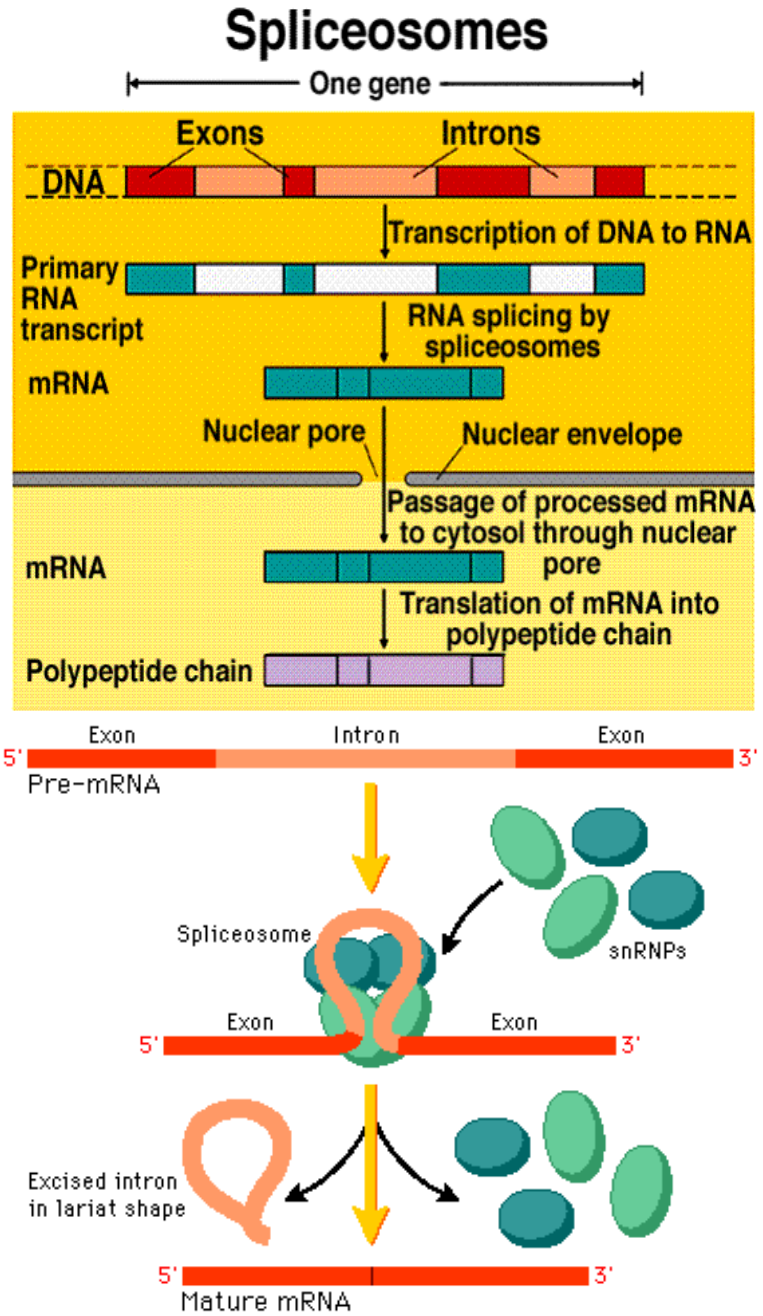


Prokaryotes→translation can occur simultaneously
Eukaryotes→mRNA must first be processed before it leaves the nucleus and carries out translation

II. RNA Processing
-2 things occur:

1. mRNA segments are removed
   -transcribed segment contains 2 kinds of sequences:
   a. exons-sequences that <u>ex</u>press code for polypeptide
   b. introns-<u>in</u>tervening sequences that are noncoding

-both are transcribed by mRNA, but only exons are translated
-introns are spliced out of mRNA before it leaves the nucleus
-both the introns and exons-everything transcribed from DNA make up the heterogeneous nuclear RNA (hnRNA)
-not much is known about this process-but we know that:
RNA splicing:
-small nuclear ribonucleoproteins (snRNPs)-found in nucleus
-RNA and proteins
-snRNPs splice introns from hnRNA leaving only the exons (what actually codes for the protein)



2. Adding cap and tail

(a) enzymes add special nucleotide sequences to both ends of the mRNA

-GTP (guanosine triphosphate) is added to the 5' end to form a 5' cap (-Pi-Pi-Pi-G-5')

-provides stability

-provides a pint of attachment for the small subunit of the ribosome

(b) Poly-A tail (-A-A-A…A-A-3')

-sequence of ~150 nucleotides (As)

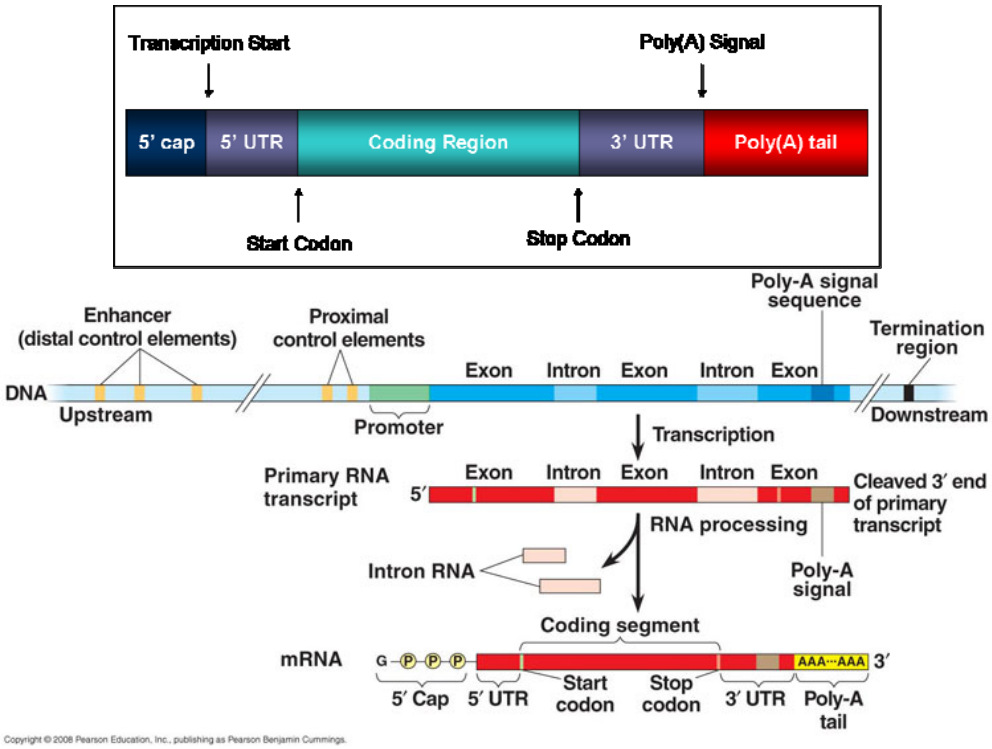
-provides stability

-controls movement of mRNA across the nuclear envelop

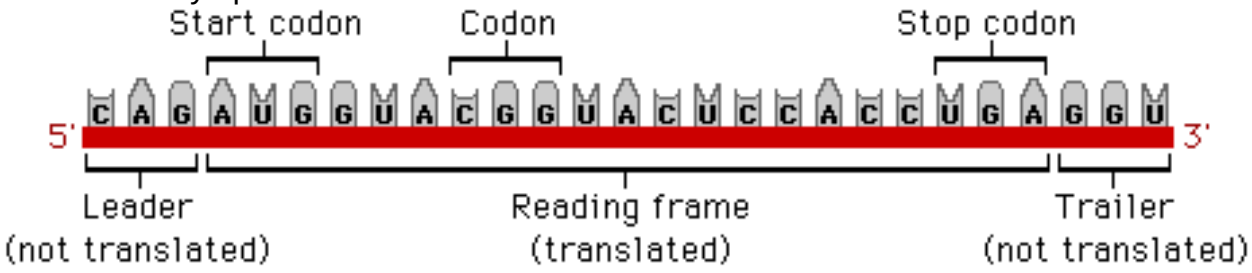
-may regulate protein synthesis by facilitating mRNA's transport from nucleus to cytoplasm-where translation occurs

After processing:

mRNA:



-leader/trailer→non coding sequence between cap and tail and coding sequence →travels to cytoplasm



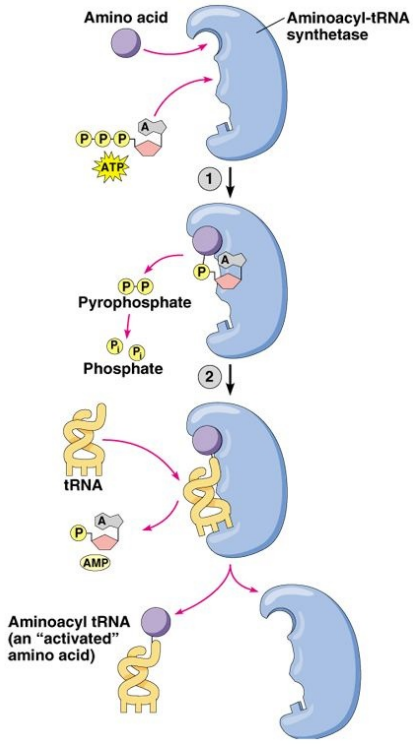
III. Translation

-mRNA, tRNA, and ribosome subunits travel across nuclear envelope to cytoplasm

-in cytoplasm, the amino acids attach to their specific tRNA-forming aminoacyl-tRNA

-requires aminoacyl-tRNA synthase-specific to certain amino acids

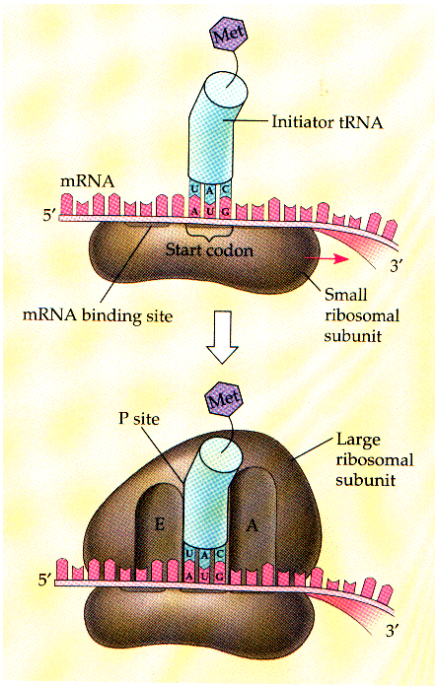
-energy from 1 ATP



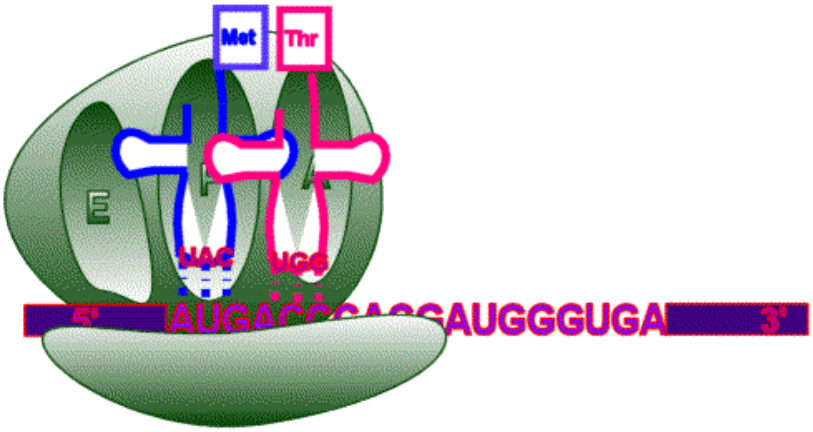
-tRNA and amino acid contain an anticodon that is complimentary to codon in mRNA strand
-20 amino acids
-64 different codons
-only 45 types of tRNA
therefore, some tRNA molecules need to recognize more than one codon
-this can occur if 1st 2 bases are complimentary and 3rd is not (in some cases)
-tRNA can still bind and drop off amino acids
-creates a "wobble"→ability of one tRNA molecule to recognize 2 or 3 different codons
-inosine, another nitrogenous base, similar to adenine, can be substituted

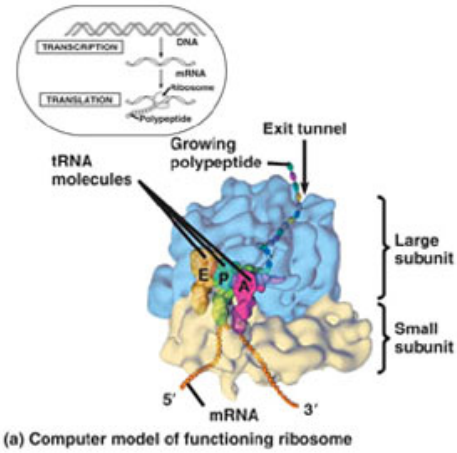
3 steps:
-energy is provided by GTP molecules (acts like ATP)

1. Initiation
-small ribosomal subunit binds to 5' end of mRNA at "start codon"-AUG (codes for amino acid methionine)
-tRNA with complimentary anticodon, UAC and methionine on 3' end H-bonds to mRNA and small subunit
-large ribosomal subunit binds to small one→complete ribosome
-tRNA is fit into the P site
-A site is vacant at first; hovers over the next 3 nucleotides-next codon

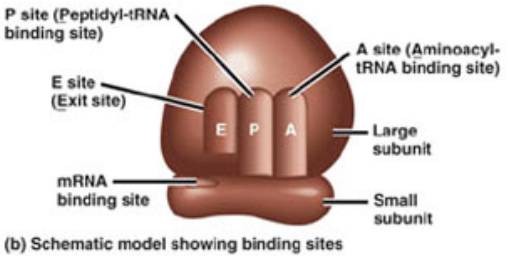


2. Elongation
   - -next tRNA H-bonds to complimentary codon
   - -fits into A site
   - -peptide bond is formed between methionine and the next amino acid by <u>peptidyl transferase</u>
     - -methionine is transferred over to other tRNA in A site
     - -tRNA molecule in P site is released at E site and it can be reused
   - -<u>ribosome moves</u> down the mRNA in 5'→3' direction
     - -tRNA in A site is shifted to P site
     - -new tRNA bonds to next codon
     - -2 amino acids are transferred and process continues

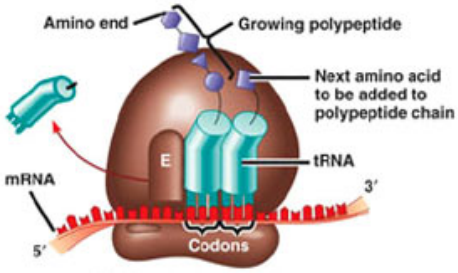




(a) Computer model of functioning ribosome

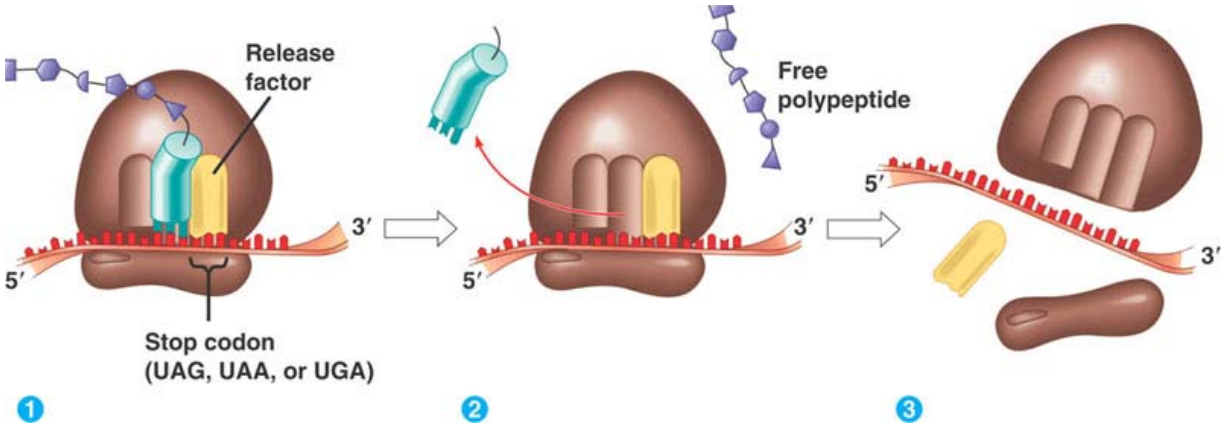


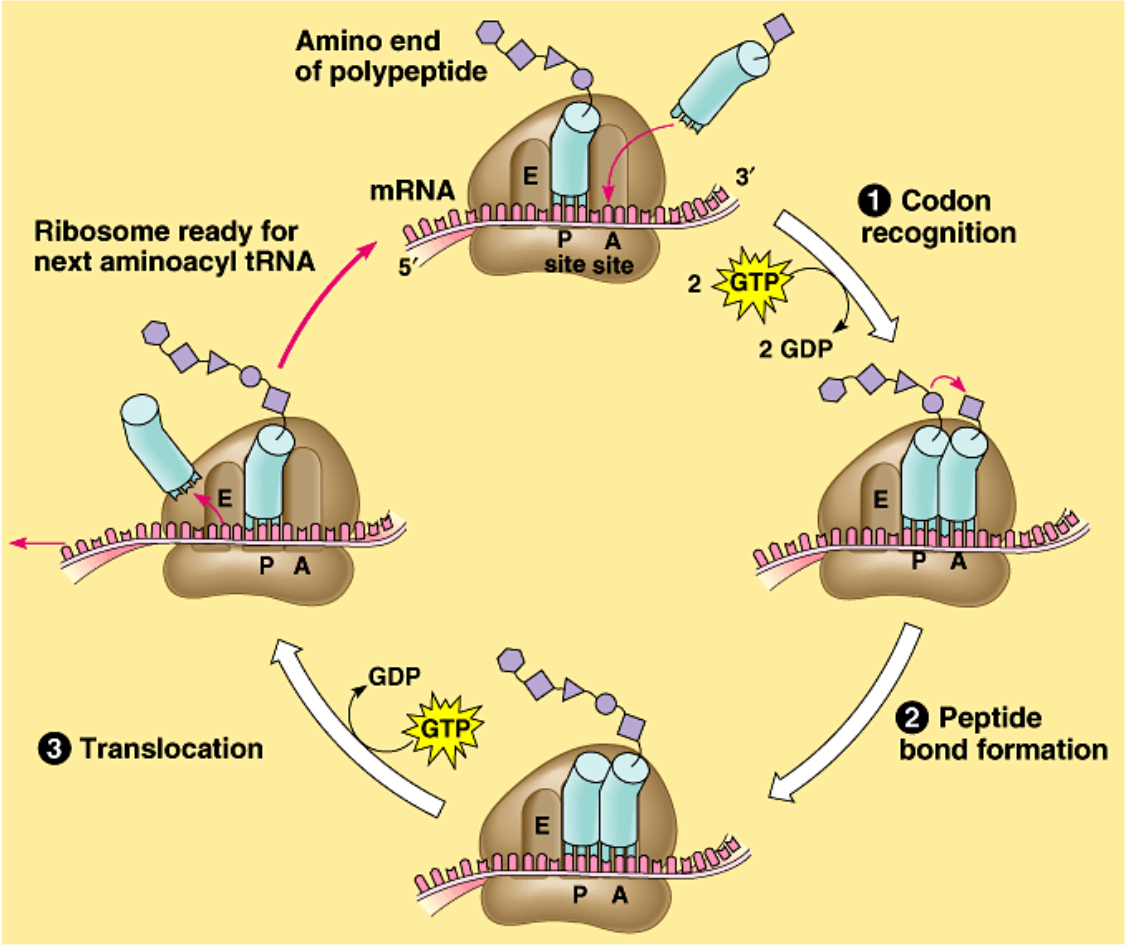
(b) Schematic model showing binding sites



(c) Schematic model with mRNA and tRNA

3. Termination
   -elongation occurs until ribosome encounters a “stop” codon
   -signals end of translation
   3 stop codons: UUA, UAG, and UGA
   -completed polypeptide, the last tRNA and 2 ribosomal subunits are released





Polypeptide→

-1^{o} structure→amino acid sequence

-once released, the chain will spontaneously coil and fold to form 2^{o} and 3^{o} structures

-after translation, proteins can:

1. have sugars, lipids, phosphate groups added to them
2. amino acids can be cleaved from leading end of chain
3. single chains can be divided into 3 or 4 pieces (ex: insulin)
4. 2 or more can join together in 4^{o} structure (hemoglobin)

Eukaryotic ribosomes→either free in cytosol or bound to ER

-structure identical and interchangeable

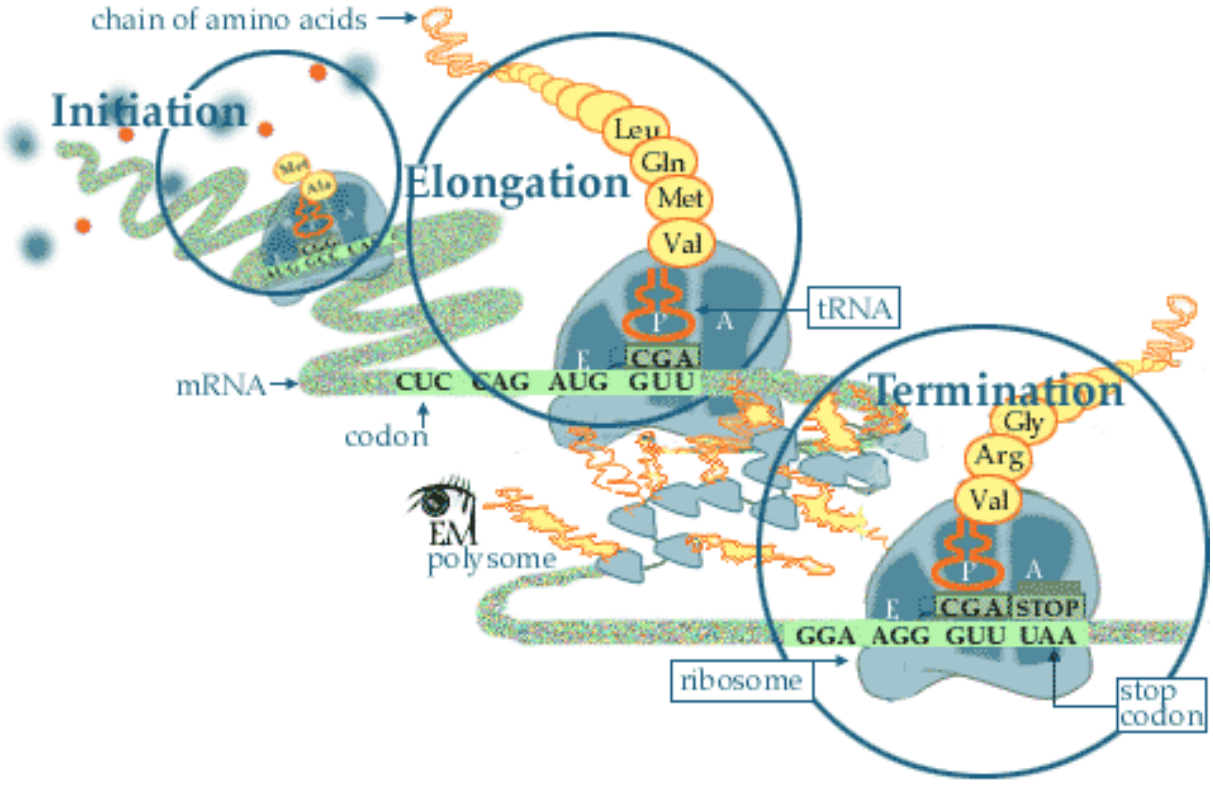
-proteins made by free:

-function in cytosol

-proteins made by bound could be:

-destined for endomembrane system (nuclear envelope, ER, Golgi, lysosomes, vacuoles, plasma membrane)

-secretory proteins destined for transport


chain of amino acids
Initiation
Elongation
Termination
Leu
Gln
Met
Val
tRNA
P
A
E
CGA
mRNA
CUC CAG AUG GUU
codon
EM
polysome
Gly
Arg
Val
CGA STOP
GGA AGG GUU UAA
ribosome
stop codon