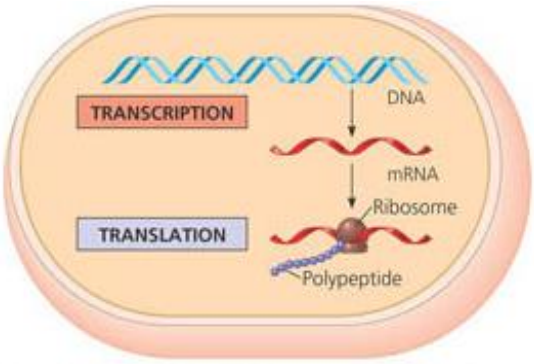
CHAPTER 17- FROM GENE TO PROTEIN

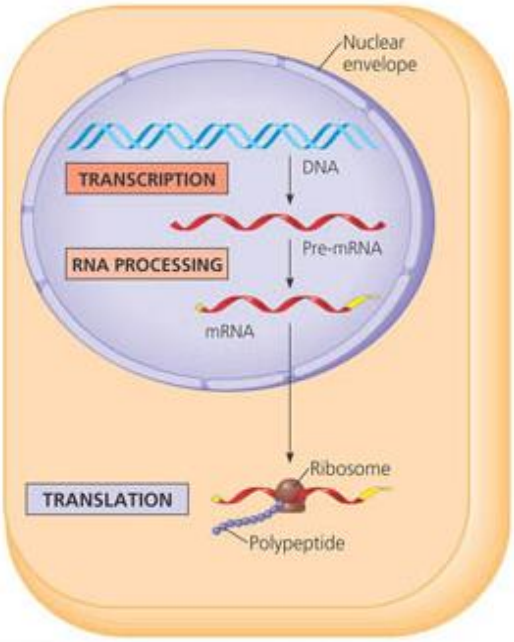
DNA → DNA = REPLICATION
DNA → RNA= TRANSCRIPTION
RNA → PROTEINS = TRANSLATION

Central Dogma of Molecular Biology
(Flow of information in cells)
DNA → RNA → PROTEINS

- **GENE** = sequence of DNA with a specific function (final product = polypeptide OR RNA)
- RNA's = intermediates between DNA code and proteins that determine phenotype
- For each gene only one of the two strands is transcribed into an RNA (template strand)
- For some genes one strand may be used; for other genes the complementary strand is used



(a) Prokaryotic cell. In a cell lacking a nucleus, mRNA produced by transcription is immediately translated without additional processing.



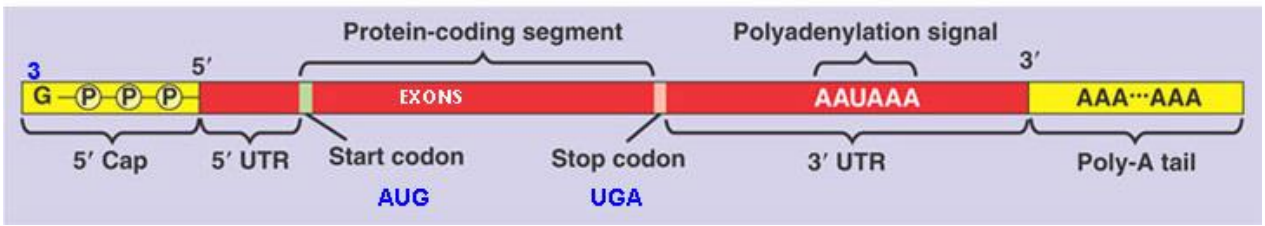
(b) Eukaryotic cell. The nucleus provides a separate compartment for transcription. The original RNA transcript, called pre-mRNA, is processed in various ways before leaving the nucleus as mRNA.

3 KINDS OF RNA

- Messenger RNA (mRNA)
- Transfer RNA (tRNA)
- Ribosomal RNA (rRNA)

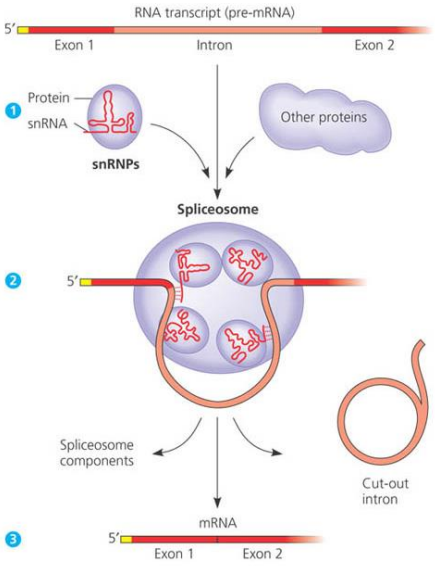
MESSENGER RNA

- carries DNA message from nucleus to cytoplasm;
  mMessage is read in "triplets" called **CODONS**
- 64 different codons code for 20 different amino acids;
  AUG = START codon; UAA, UAG, UGA are STOP codons;
- **REDUNDANCY OR "WOBBLE"** - codons for same amino acid can differ in 3rd base
- Code = universal to all life (found in all organisms) = evidence for common ancestry
- Prokaryotes~ m-RNA functional as soon as transcribed
- Eukaryotes~ m-RNA must be processed before use
  GTP "cap" = METHYLATED GUANINE added to 5' end; for stability;
  prevents degradation used to bind mRNA to ribosome
  PolyA "tail" added to 3' end (AAA)- stability; helps passage through nuclear membrane



In **EUKARYOTES mRNA** is made as **pre-mRNA** containing:

- **INTRONS**- noncoding DNA segments
  may provide cross over places without interrupting code
  may facilitate evolution of new proteins by *exon shuffling*
- **EXONS** - coding DNA segments; code for different **DOMAINS**
  =structural/functional regions

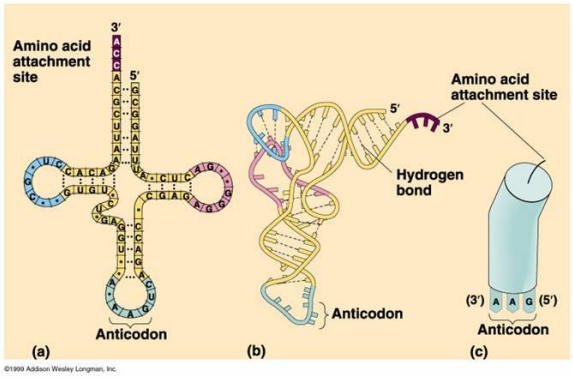


snRNPs (small nuclear ribonucleoproteins)

- Made of proteins and RNA
- Part of **SPLICEOSOME** (complex that edits pre-mRNA
  cuts out the introns and reattaches the remaining mRNA

ALTERNATIVE RNA SPLICING-
can produce different proteins by editing mRNA in different ways
EX: Immunoglobulins (antibodies) that match new antigens

RIBOZYMES = RNA molecules that function as enzymes
EX: Some preRNA's can self edit own introns;



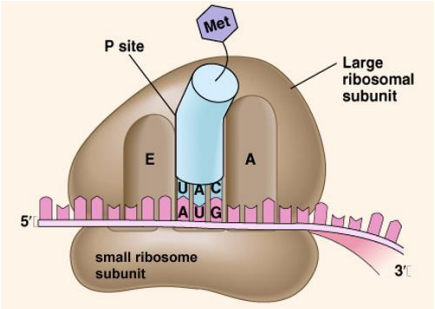
TRANSFER RNA (tRNA)

- cloverleaf-like secondary structure folds into L shape
- brings amino acids to ribosome
- attaches amino acids in proper place
- **ANTICODON** region matches codon on mRNA

AMINOACYL-tRNA SYNTHETASE enzyme
attaches a specific amino acid using energy from ATP

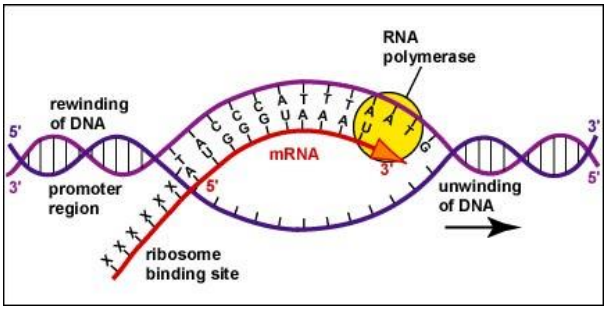
RIBOSOMES (=RYBOZYMES RNA that functions as an enzyme)

- Made up of **rRNA** (2/3) and **PROTEINS** (1/3) ;
- rRNA **made in NUCLEOLUS** in eukaryotes and assembled with proteins imported from cytoplasm
- **Large and small subuits** join to form functional ribosome only when attach to mRNA;
- Ribosomes not making proteins exist as separate subunits
- Ribosomes making proteins for membranes/export: proteins are "tagged" so can be attached to rough ER;
- Cytoplasmic proteins made on "free" ribosomes
- Prokaryotic and eukaryotic subunits are different sizes = evidence for Endosymbiotic theory
  (PROKARYOTIC RIBOSOMES: 30S + 50S = 70S; EUKARYOTIC RIBOSOMES: 40S + 60S = 80S)
- Subunit size is medically significant
  ~ Certain antibiotics work by inhibiting prokaryotic ribosomes without affecting ribosomes of the eukaryotic host cell



RIBOSOME BINDS mRNA
Has **3 tRNA BINDING SITES:**
A (AMINOACYL-tRNA site)- tRNA with new **a**mino acid **a**ttaches
P (PEPTIDYL-tRNA site) – **p**eptide bond forms
holds tRNA carrying growing **p**olyeptide chain;
E (EXIT site) - **e**mpty tRNA **e**xits

TRANSCRIPTION = DNA → RNA (Occurs in the NUCLEUS)



1. **INITIATION**
   - **RNA POLYMERASE** binds to DNA at region called **PROMOTER**
     LIKE DNA POLYMERASE: can only attach nucleotides in 5' → 3' direction;
     UNLIKE DNA POLYMERASE: can start a chain from scratch; no primer needed
   - In eukaryotes: **TRANSCRIPTION FACTORS & TATA BOXES** help position/bind to correct spot
   - RNA POLYMERASE separates the DNA strands to begin transcription
2. **ELONGATION**
   - RNA chain **grows in the 5' → 3' direction**' nucleotides base pair with template strand; nucleotides **added to the 3' end of preceding nucleotide** (60 nucleotides/sec)
   - the non-coding strand of DNA reforms a DNA double helix by pairing with the coding strand
3. **TERMINATION**
   - transcription proceeds until RNA polymerases reaches a **TERMINATOR** site on the DNA;
   - RNA molecule is then released
   - Segment of DNA transcribed into one RNA = **TRANSCRIPTION UNIT**

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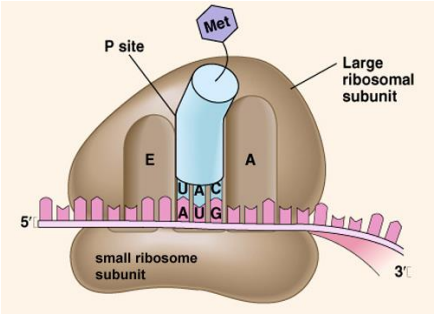
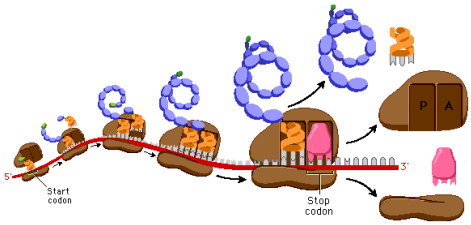
TRANSLATION = RNA → PROTEINS (Occurs on RIBOSOMES in CYTOPLASM)

Specific **AMINO ACYL tRNA SYNTHETASES** added amino acids to correct tRNA's

1. **INITIATION**
   - **Small ribosomal subunit** attaches to the **5' end** of the mRNA (**'start' codon - AUG**)
   - **energy comes from GTP** (guanosine triphosphate)
   - tRNA carries **1st amino acid (METHIONINE)** to the mRNA
   - **large ribosomal subunit** attaches to the mRNA

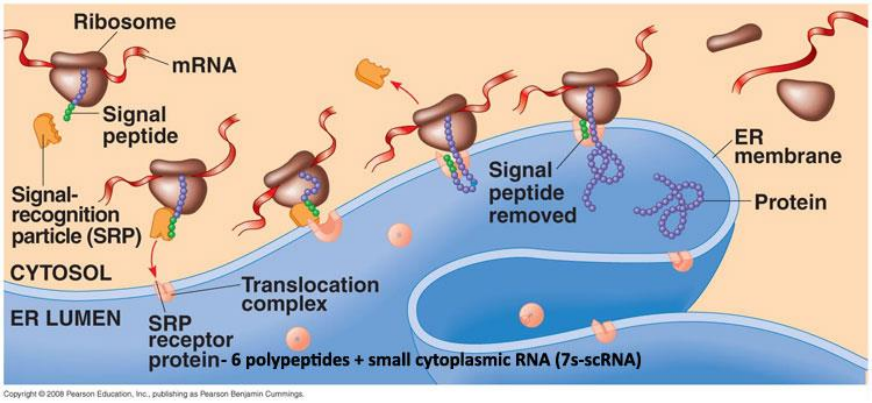


2. **ELONGATION**
   - Ribosome moves along mRNA matching **tRNA ANTICODONS** with **mRNA CODONS**
   - tRNA with new amino acid attaches at A site
   - tRNA at A site moves to P site and receives growing chain
   - tRNA a P site moves to E site and exits
   - Released tRNA can recycle and bring in a new amino acid
   - a new tRNA enters the A site and repeats the process increasing the polypeptide chain length
3. **TERMINATION**
   - occurs when the ribosome encounters a 'stop' codon
   - ribosome subunits detach; polypeptide is released
   - mRNA can be reread multiple time
   - **POLYSOMES**- = strings of ribosomes can work on same mRNA at same time



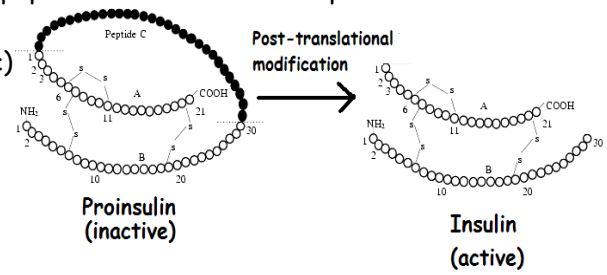
SIGNAL-RECOGNITION PARTICLE (SRP)

Protein synthesis begins on free ribosomes
Polypeptides that will **become MEMBRANE PROTEINS** or **be SECRETED** are marked
SRP (SIGNAL RECOGNITION PARTICLE) attaches to protein signal sequence and receptor on ER
Growing protein chain is inserted into ER lumen
Complex disconnects



POST TRANSLATIONAL MODIFICATION - Changes to polypeptide chain to make it a protein

- **CHAPARONINS**-help wrap into 3D shape
- Some have groups added (sugars, lipids, phosphates, etc)
  EX: glycoproteins (protein + sugar)
- Some have segments removed
  EX: insulin made as one chain
  middle removed to become active



MUTATIONS

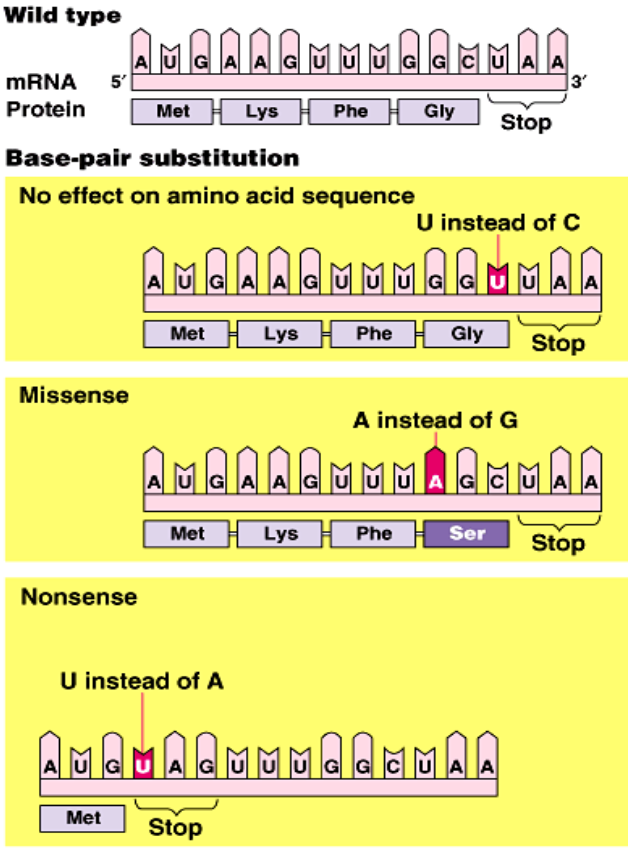
- Not all harmful- can **PROVIDE GENETIC VARIABILITY**
  ~Foundation for **NATURAL SELECTION**

Can be:

- Spontaneous (errors in replication, repair, recombination)
- Caused by **MUTAGENS**
  EX: radiation, chemicals, cigarette smoke, etc
  = **CARCINOGENS** (can cause cancer)

HARMFUL MUTATIONS- change protein function

- **POINT** mutation: change in one base pair of a gene
  Substitution- replace one base with another
- **SILENT**- change codes for same amino acid
  (due to redundancy)
- **MISSENSE**-codes for another amino acid
  Changes protein sequence and usually function
  Ex: sickle cell disease- T → A in hemoglobin
- **NONSENSE**-code changes to STOP codon
  makes NONFUNCTIONAL protein



FRAMESHIFT

- All nucleotides downstream are grouped incorrectly;
- **INSERTION/DELETION**-causes FRAMESHIFT
  if not a multiple of 3
- Causes more damage at beginning of gene than at end
  EX: O blood type allele is deletion in A blood type code