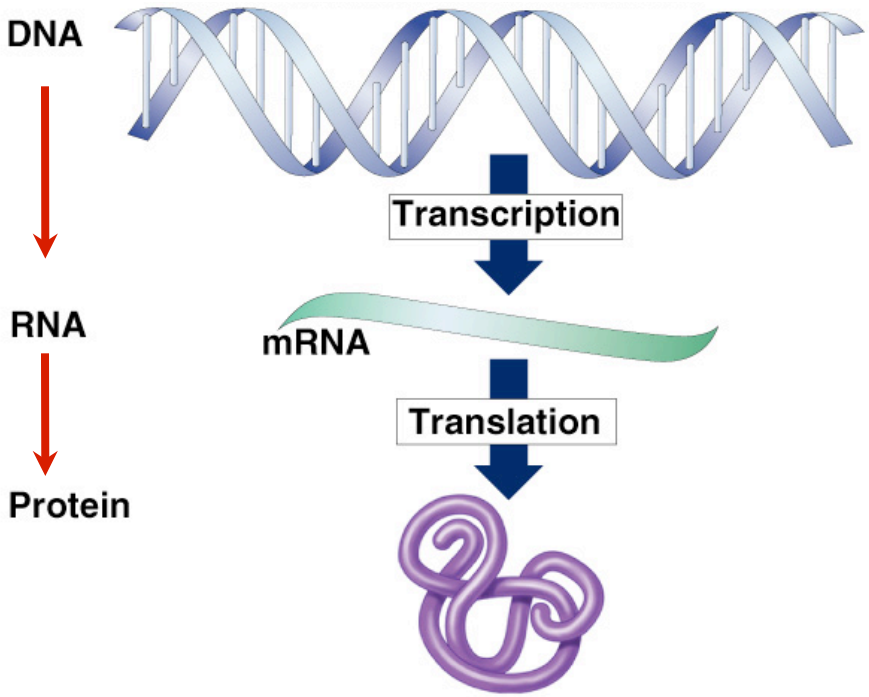
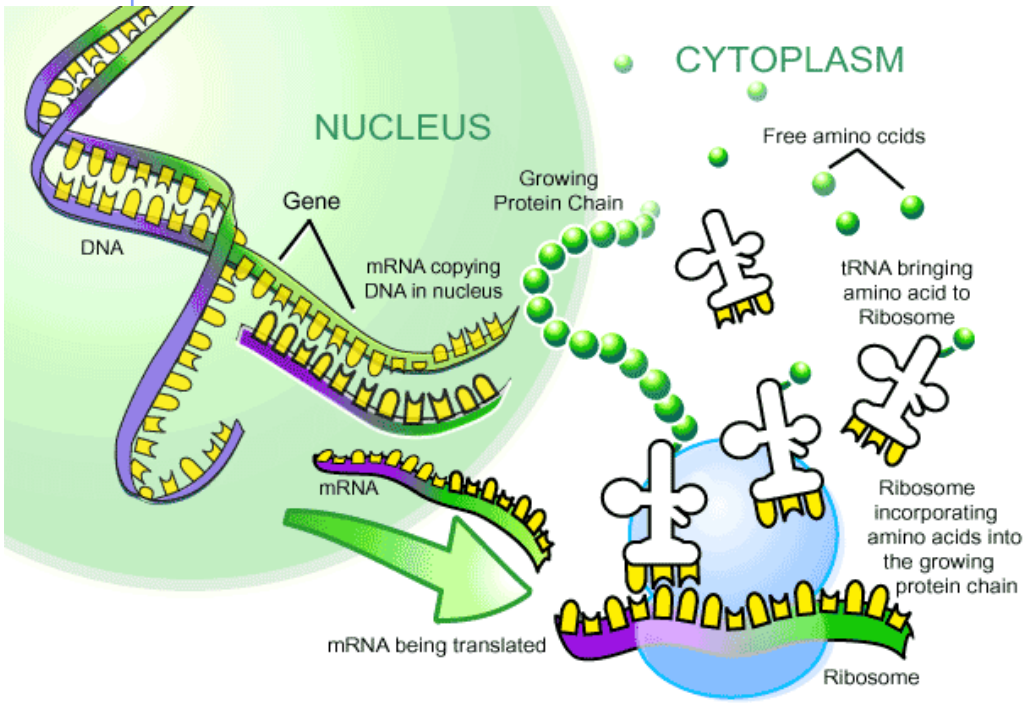
From Gene to Protein

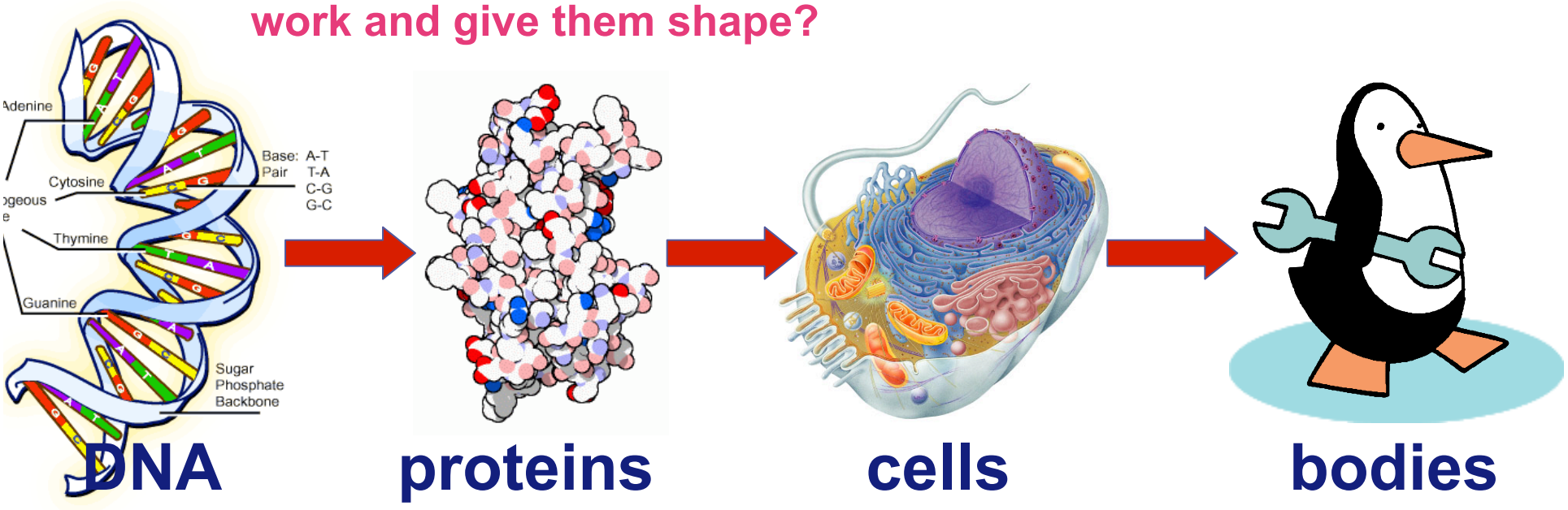




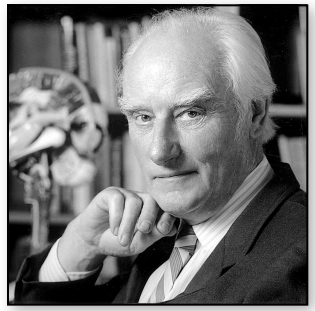
How Genes Work

What do genes code for?

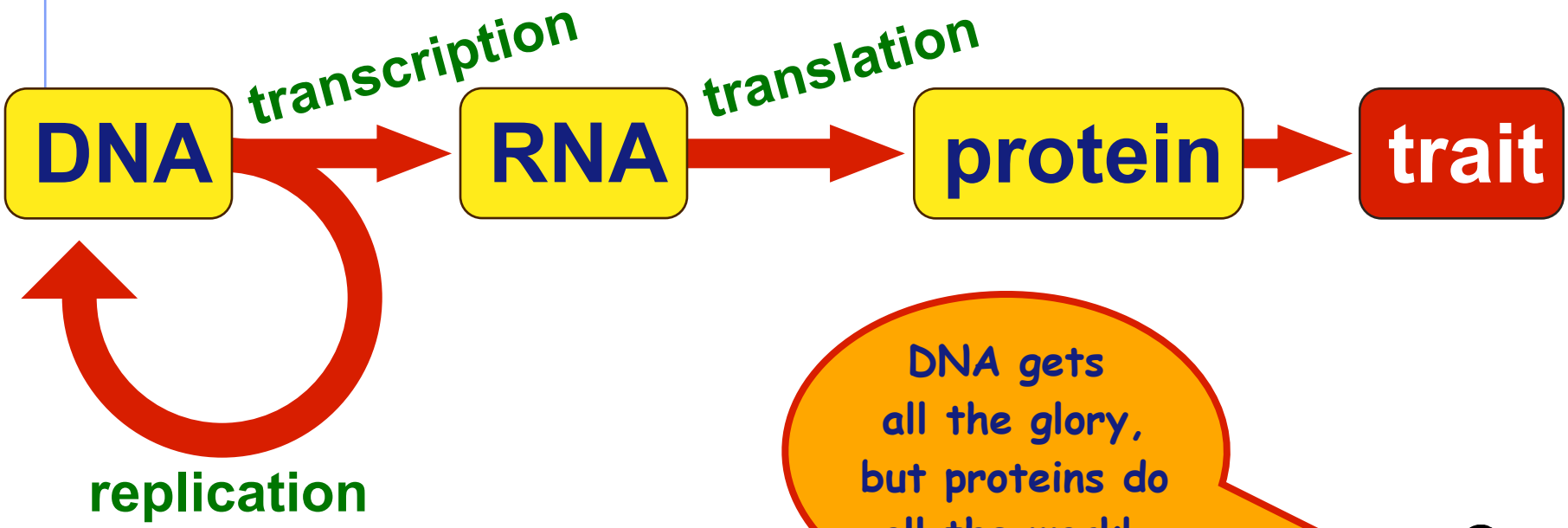
- **Once scientists determined that phenotype-production and inheritance requires DNA, they wondered what DNA actually does.**
  - **Once we figured out that DNA contains the instruction for making PROTEINS AND RNA molecules, they wondered how DNA code for the proteins that help cells & bodies work and give them shape?**



The "Central Dogma"

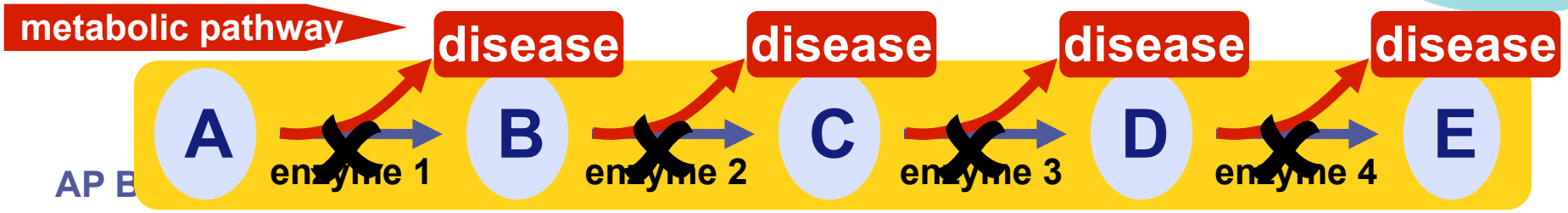


- Flow of genetic information in a cell
  - How do we move information from DNA to proteins?



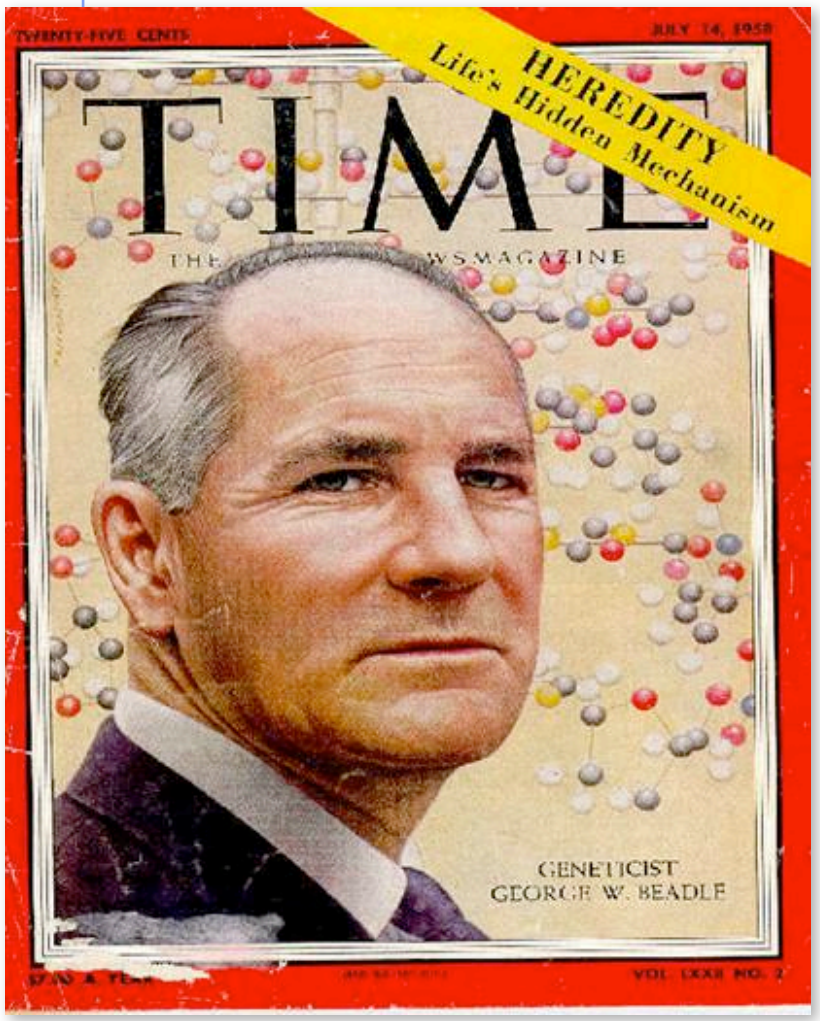
Studying errors in metabolism started giving us information about what genes (DNA) do.

- Studies on inherited metabolic diseases
  - suggested that genes coded for enzymes
  - each disease (phenotype) is caused by non-functional gene product
    - lack of an working enzyme
      - Tay Sachs
      - PKU (phenylketonuria)
      - Albinism



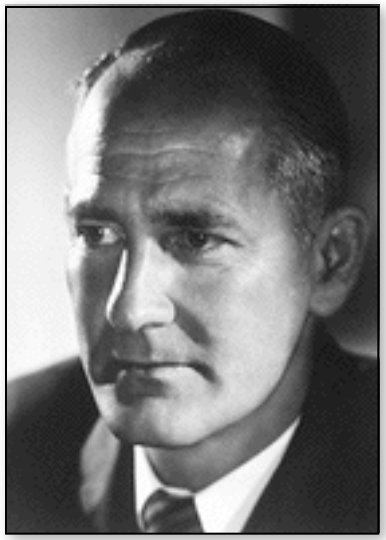
Beadle & Tatum

1941 | 1958



AP Biology

one gene - one enzyme hypothesis



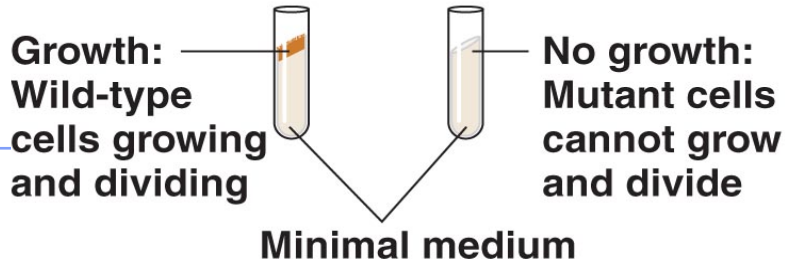
George Beadle

Edward Tatum

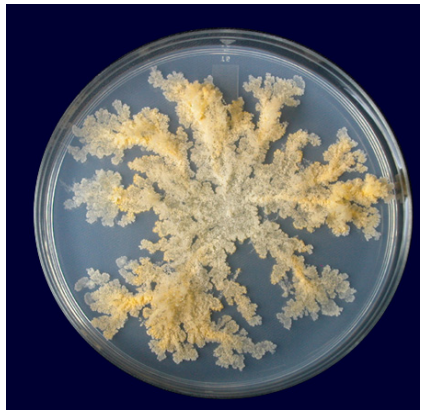
"for their discovery that genes act by regulating definite chemical events"

EXPERIMENT

Beadle & Tatum's work with *Neurospora crassa*



- **Wild type bread mold:** grows on minimal growth medium
  - Agar with inorganic salts, glucose, & biotin
    - Mold can use their metabolic pathways to synthesize all the other molecules they need to survive & grow (including all amino acids and vitamins)

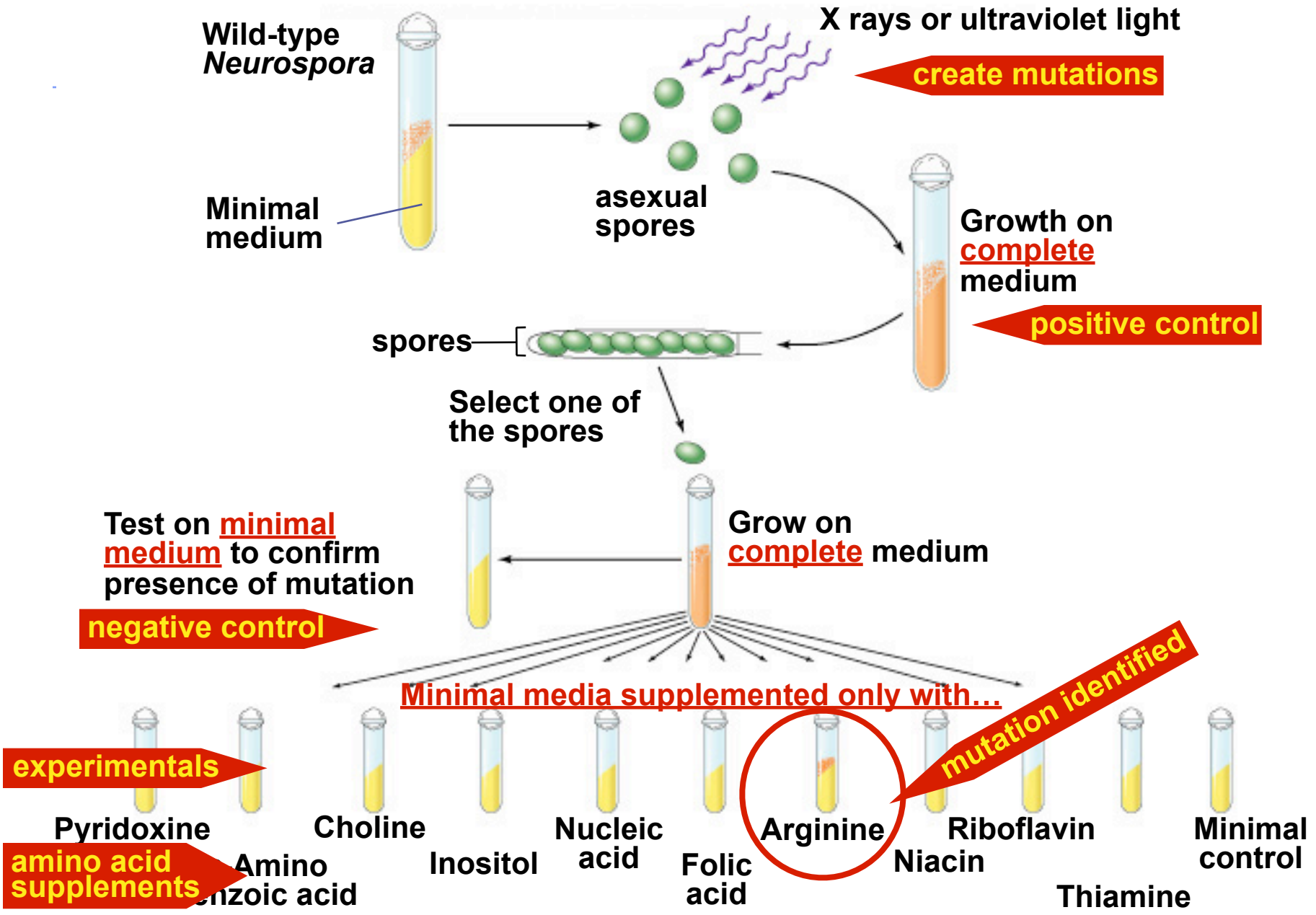


- They then purposefully damaged bread mold DNA and then identified **mutants** that could only grow on **complete** **medium**
  - Medium with all 20 amino acids & vitamins: all molecules that the mold could no longer produce with the help of the minimal medium nutrients alone
- Finally, they identified all the mutants that could not grow on **minimal medium** and needed to be supplemented **ONLY** with **arginine** *(instead of all 20 amino acids and extra nutrients)*

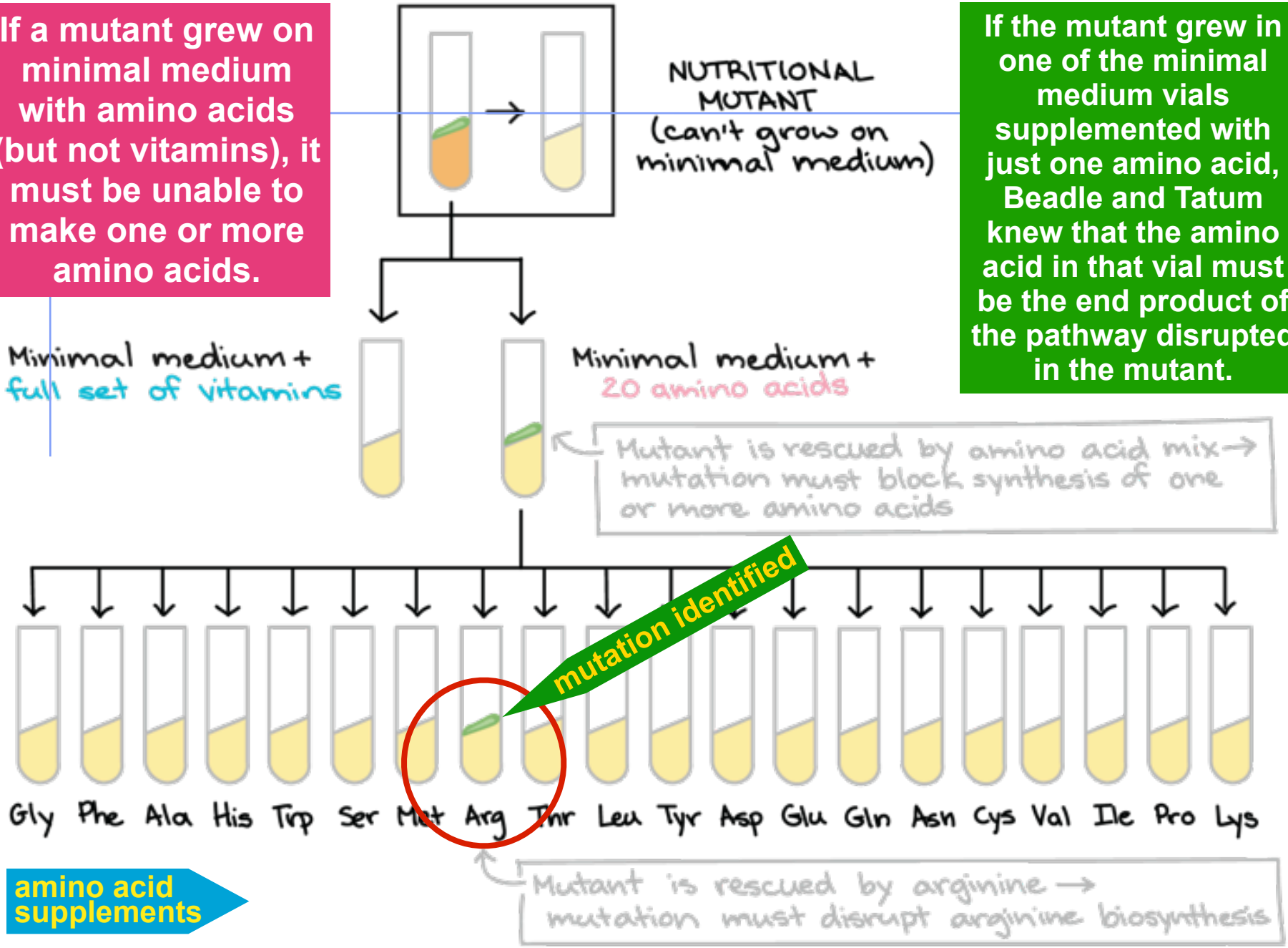
Beadle & Tatum hypothesized that DNA contained the instructions for making enzymes.

- They narrowed the mutants down to 3 types of arginine-requiring mutants, which had damage in different areas of their DNA, noting that:
  - Each class of arginine-requiring mutant now required supplementation with a different compound along the arginine-synthesizing biochemical pathway, *which involves 3 steps (3 chemical reactions),* in order to produce the arginine amino acid final product needed for the mold to survive.
    - Beadle & Tatum data thus supported the hypothesis that each mutant must be blocked at a different step in this arginine-making biochemical pathways because the DNA damage caused them to now lack a key working enzyme needed to complete that biochemical step.

Beadle & Tatum



If a mutant grew on minimal medium with amino acids (but not vitamins), it must be unable to make one or more amino acids.



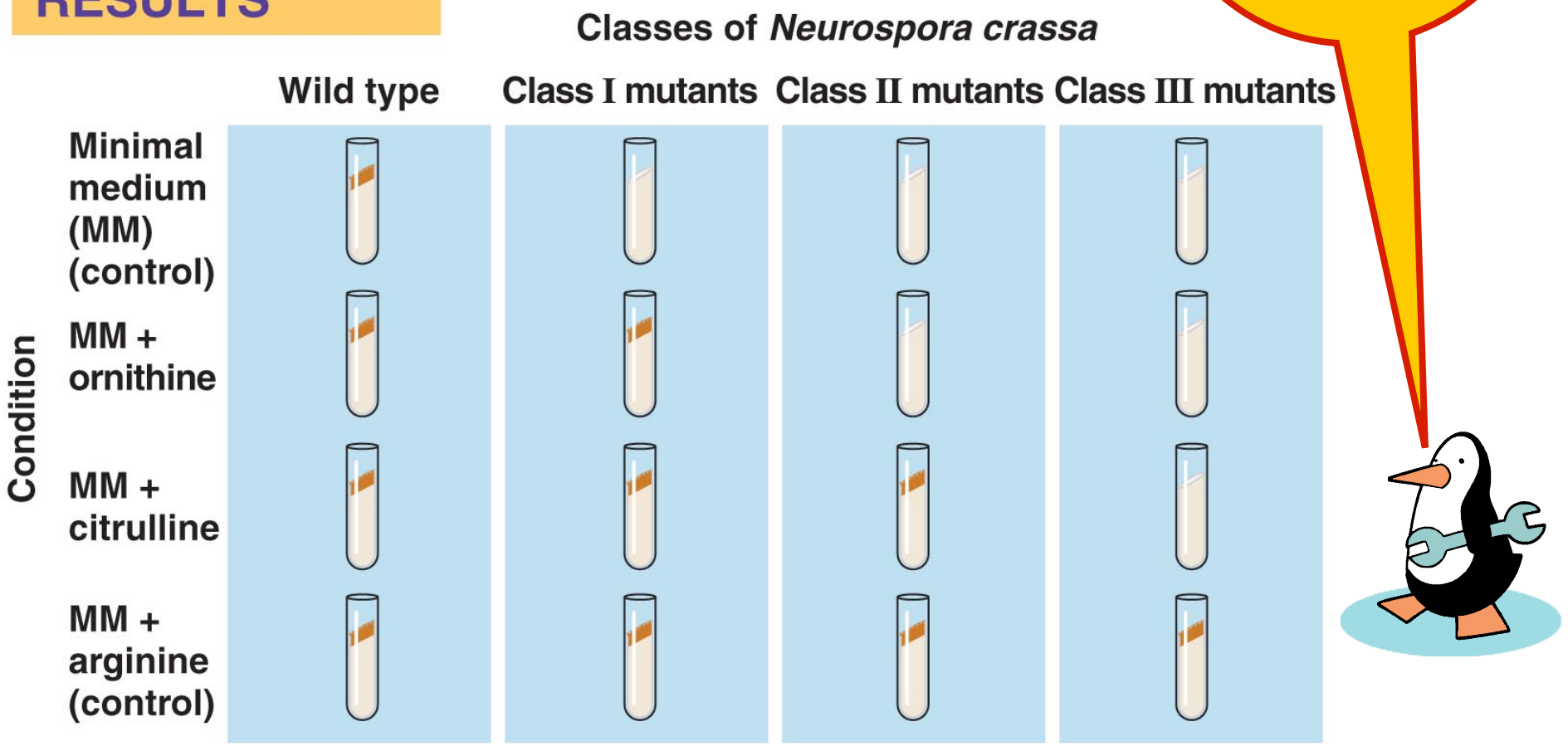
If the mutant grew in one of the minimal medium vials supplemented with just one amino acid, Beadle and Tatum knew that the amino acid in that vial must be the end product of the pathway disrupted in the mutant.

Beadle & Tatum

They grew the 3 classes of arginine-requiring mutants on different media (each containing minimal medium PLUS one of the precursor nutrients or one of the intermediate molecules ornithine or citrulline

Can you hypothesize the order of the intermediate molecules on the road to arginine production?

RESULTS



Beadle & Tatum

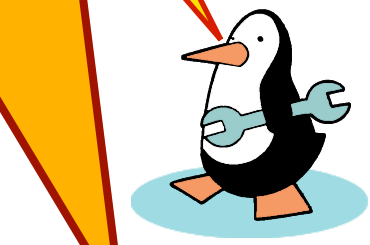
Beadle & Tatum:

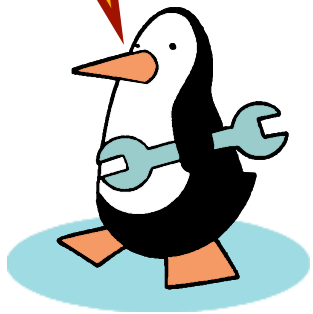
ONE GENE - ONE ENZYME HYPOTHESIS

So what was DNA used for in the cell?

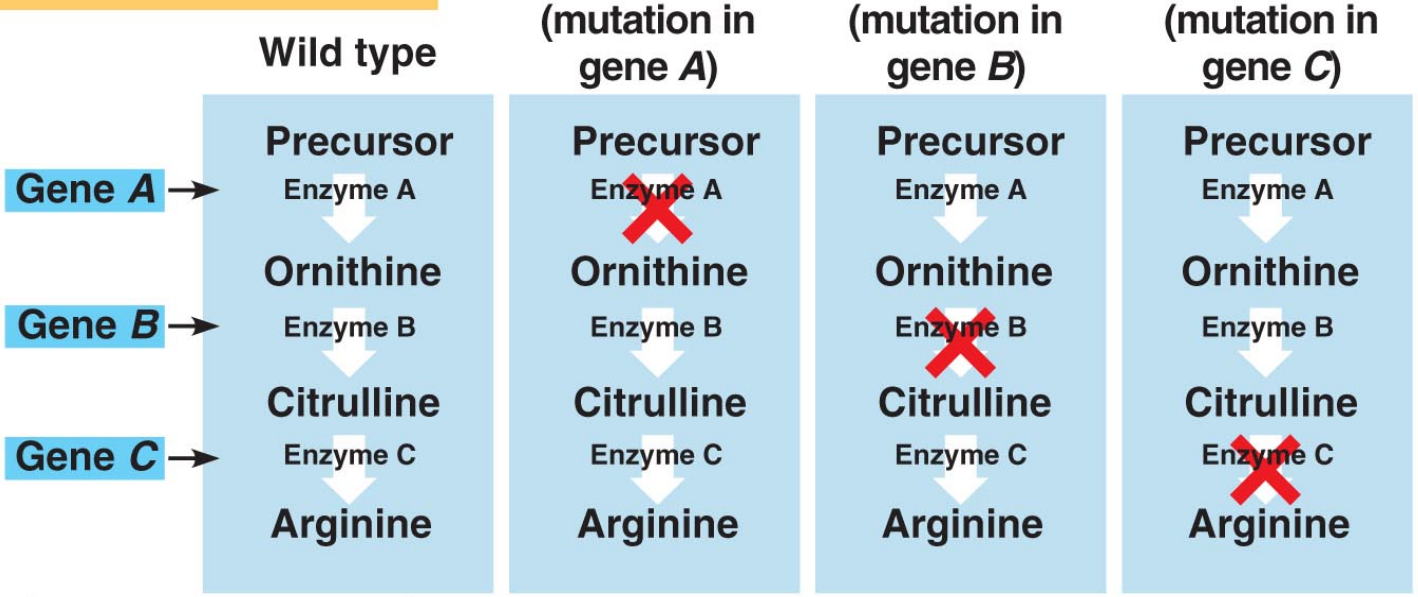
They concluded that each mutant was mutated in a single gene that coded for a key enzyme in the arginine biosynthesis pathway.

Later this hypothesis was revised into the one gene - one protein and then the **one gene - one polypeptide hypothesis**





CONCLUSION



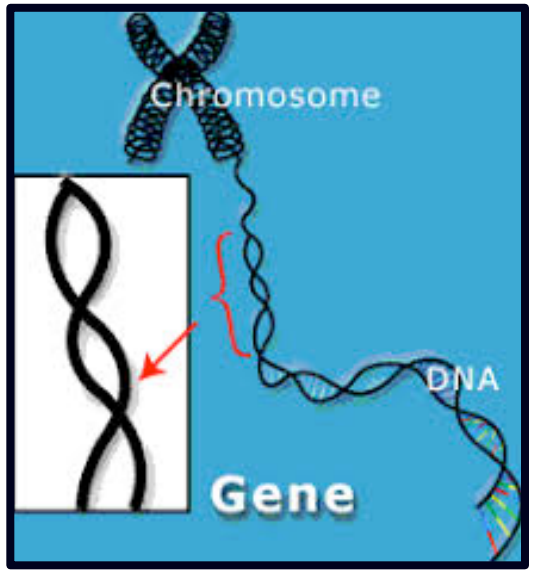
What do we think of "One gene-one enzyme" today

- **The initially discovered link between genes and enzymes was called the "one gene-one enzyme" hypothesis. This hypothesis has undergone some important updates since Beadle and Tatum**

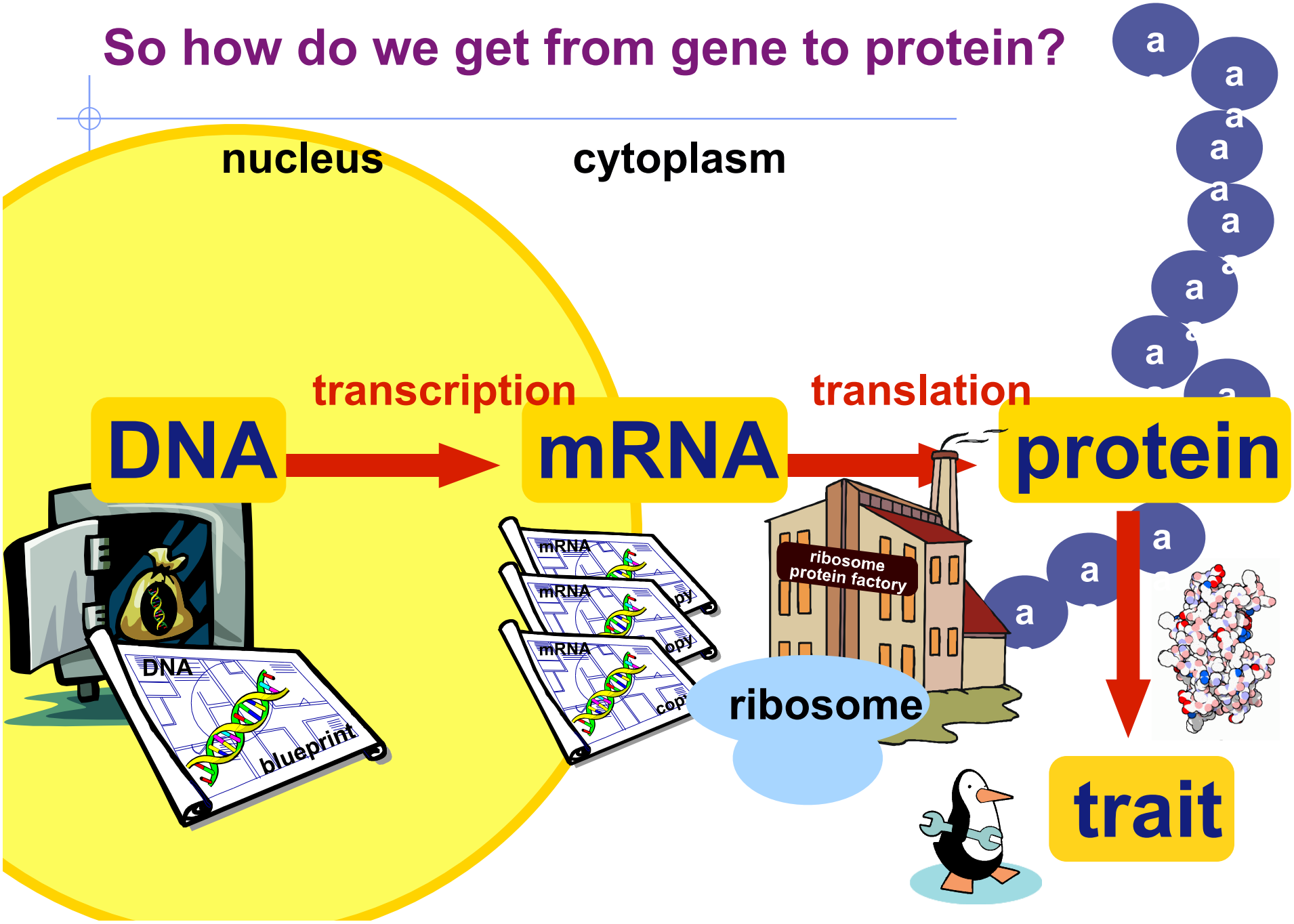
1. **Some genes encode proteins that are not enzymes. Enzymes are just one category of protein.**

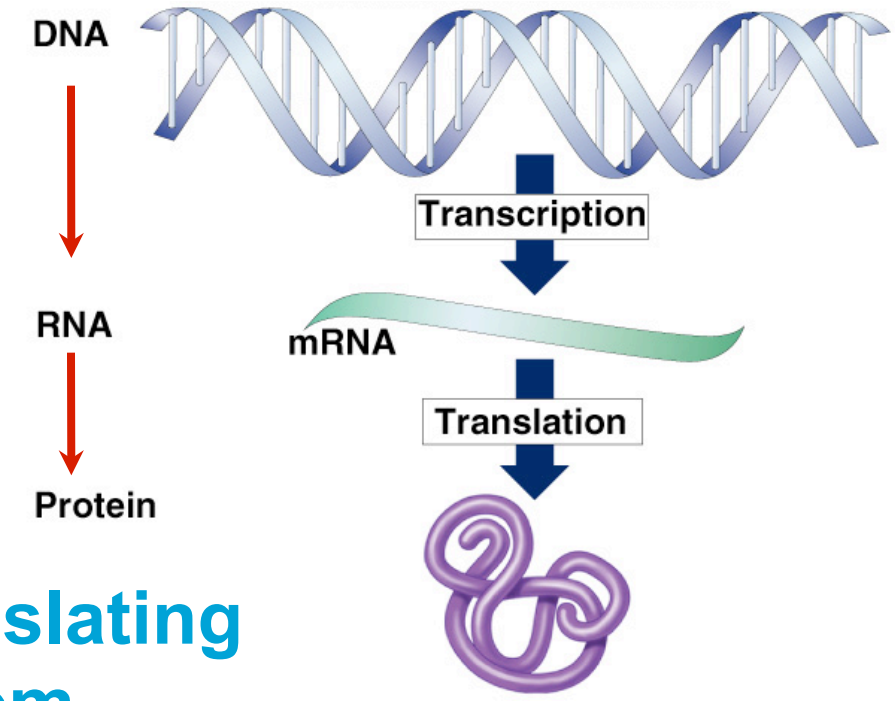
2. **Some genes encode a subunit of a protein, not a whole protein. In general, a gene encodes one polypeptide, meaning one chain of amino acids. Some proteins consist of several polypeptides from different genes.** ***one gene sometimes can even encode many different versions of a polypeptide - stay tuned!)***

3. **Some genes don't encode polypeptides. Some genes actually encode functional RNA molecules rather than polypeptides.**



So how do we get from gene to protein?





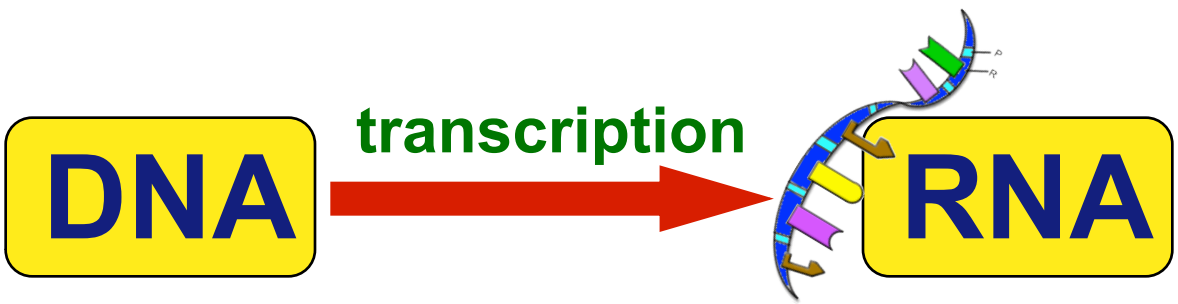
Transcription:

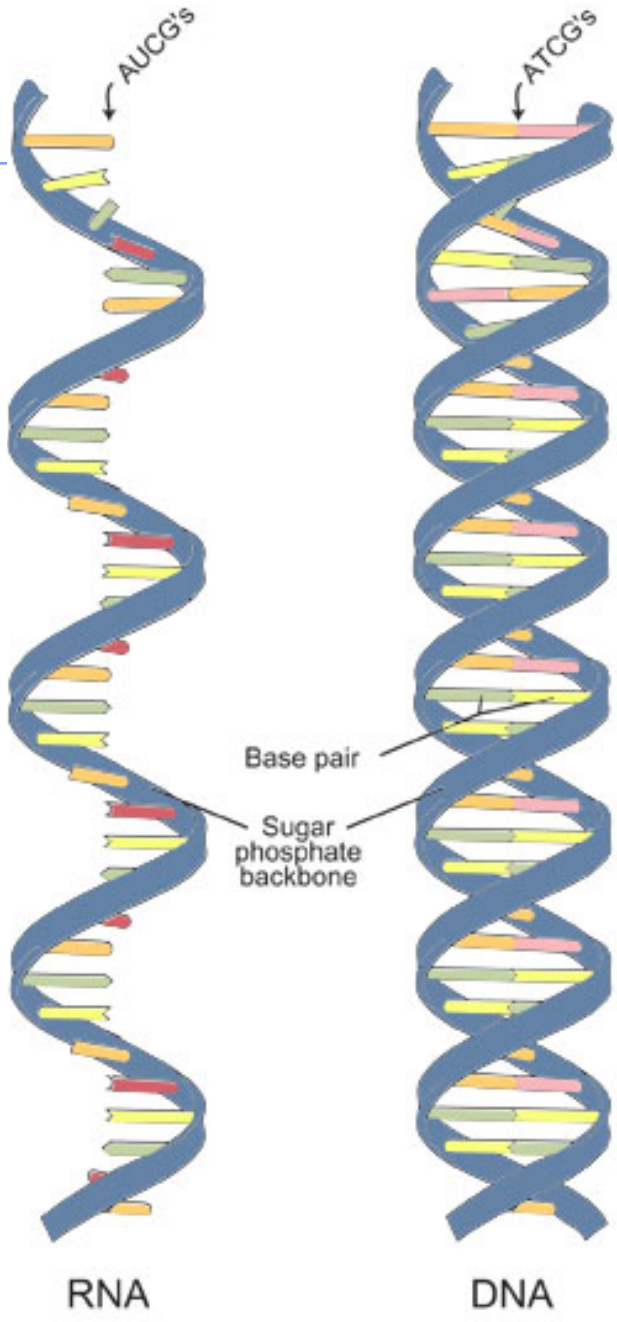
The process of translating information from

DNA nucleic acid language to RNA nucleic acid language

RNA

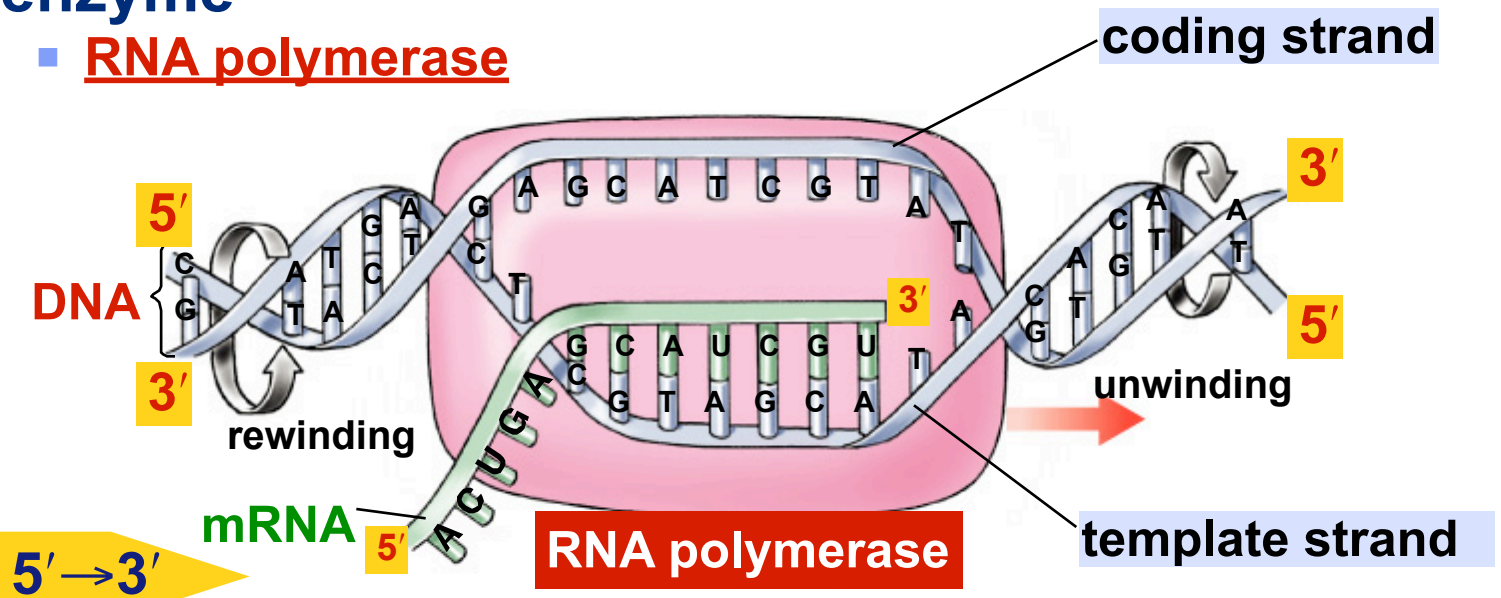
- ribose sugar
- Nitrogenous bases used
  - Uracil instead of thymine
    - U :: A
    - C ::: G
- single stranded
- Many types RNAs exist
  - mRNA, tRNA, rRNA, siRNA…





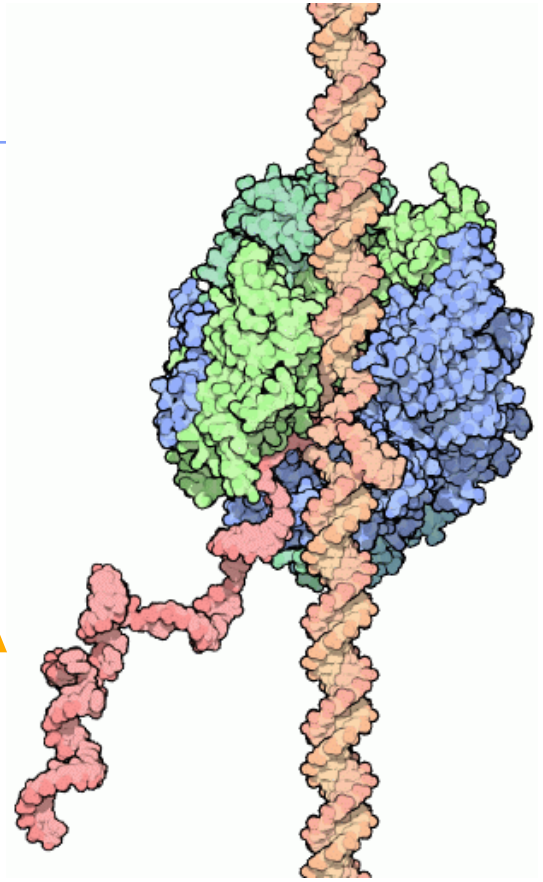
Transcription

- **Making mRNA**
  - transcribed DNA strand = template strand
  - untranscribed DNA strand = coding strand
    - same sequence as RNA transcribed except with T not U
  - synthesis of complementary RNA strand
    - transcription bubble forms starting with initiation, lasts through elongation and closes again with termination
  - enzyme
    - RNA polymerase



RNA polymerases

- 3 RNA polymerase enzymes
  - RNA polymerase 1
    - only transcribes rRNA genes
      - Components of ribosomes
  - RNA polymerase 2
    - transcribes protein genes into mRNA
  - RNA polymerase 3
    - only transcribes tRNA genes

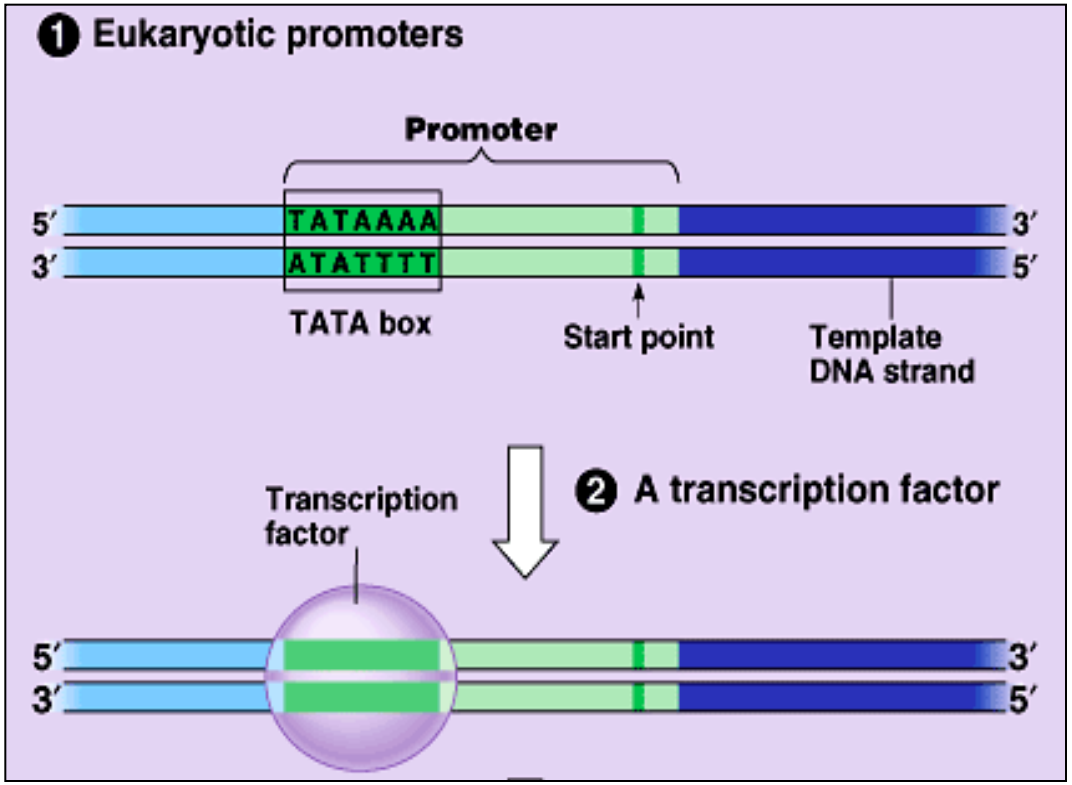


- each polymerase has a specific PROMOTOR sequence it recognizes *where it binds to the DNA slightly ahead of the gene it is going to transcribe*

Which gene is read?

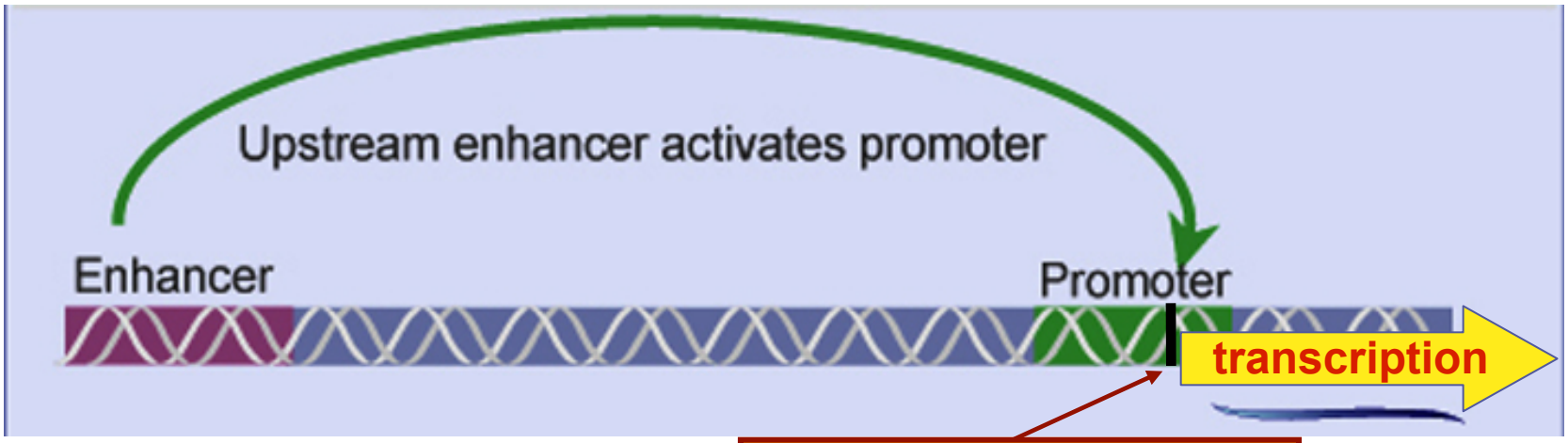
- **Promoter region**
  - DNA sequence that serves as the binding site for RNA Polymerase upstream from the beginning of gene

- **In Eukaryotes:**
  - Promoters include TATA box binding site
    - binding site for RNA Pol II & transcription factors that form the transcription initiation complex which initiates transcription



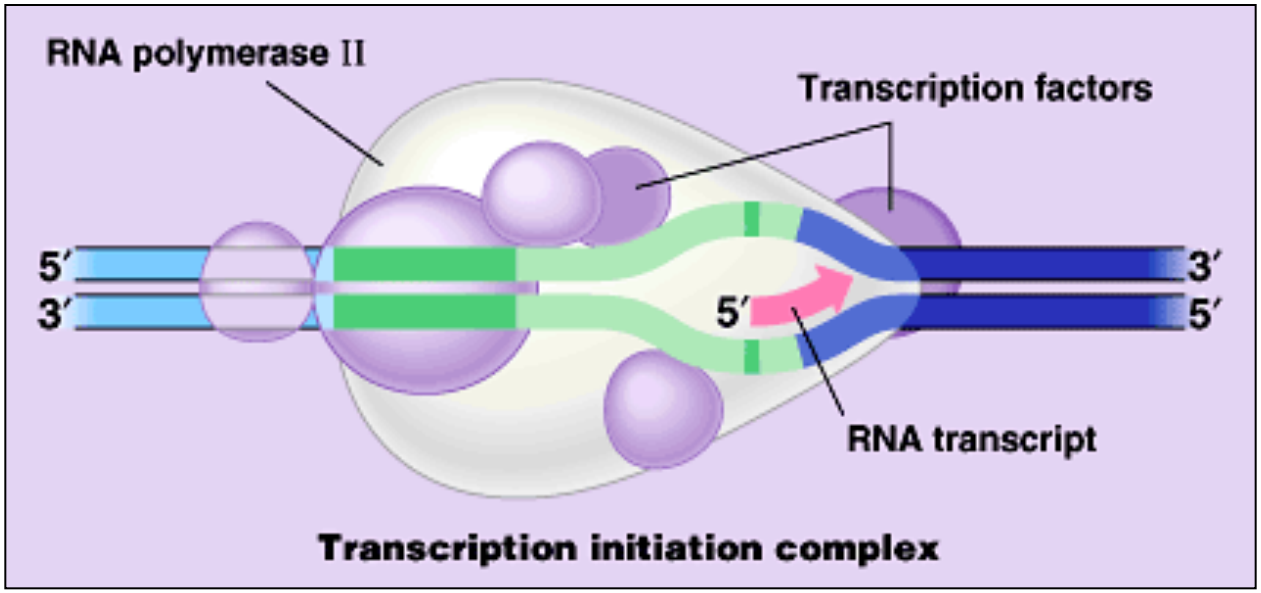
Enhancers

- In Eukaryotes
  - Enhancer region:
    - binding site far upstream of a gene
      - turns transcription on HIGH
- Transcription begins at the Start Point within the promoter region



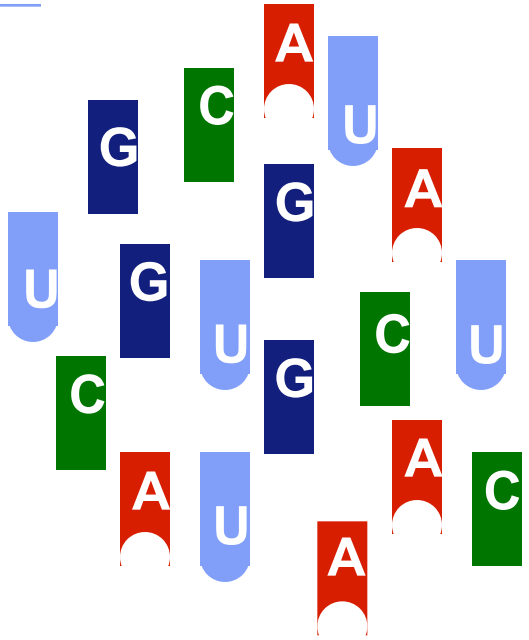
Transcription Factors

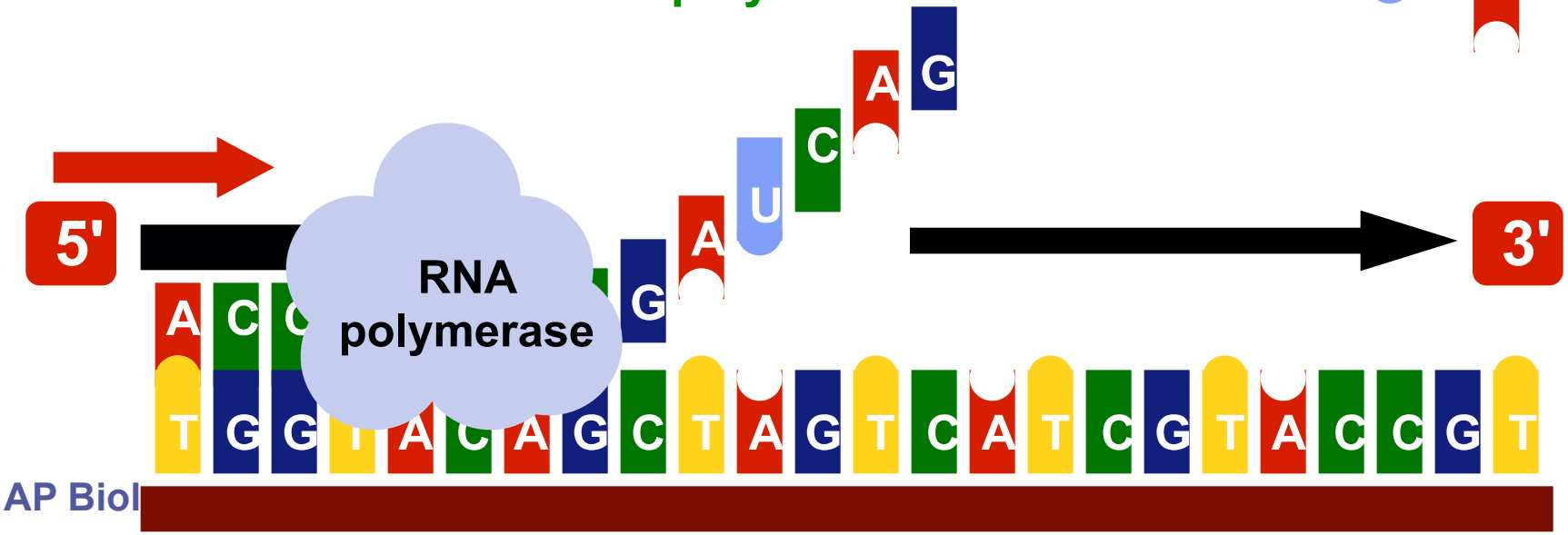
- **Initiation complex**
  - **transcription factors bind to promoter region**
    - suite of proteins which bind to DNA
    - turn on or off transcription
  - **trigger the binding of RNA polymerase to DNA**
    - Once complex assembled, DNA unwinds and RNA synthesis begins



Elongation: Matching bases of DNA to RNA

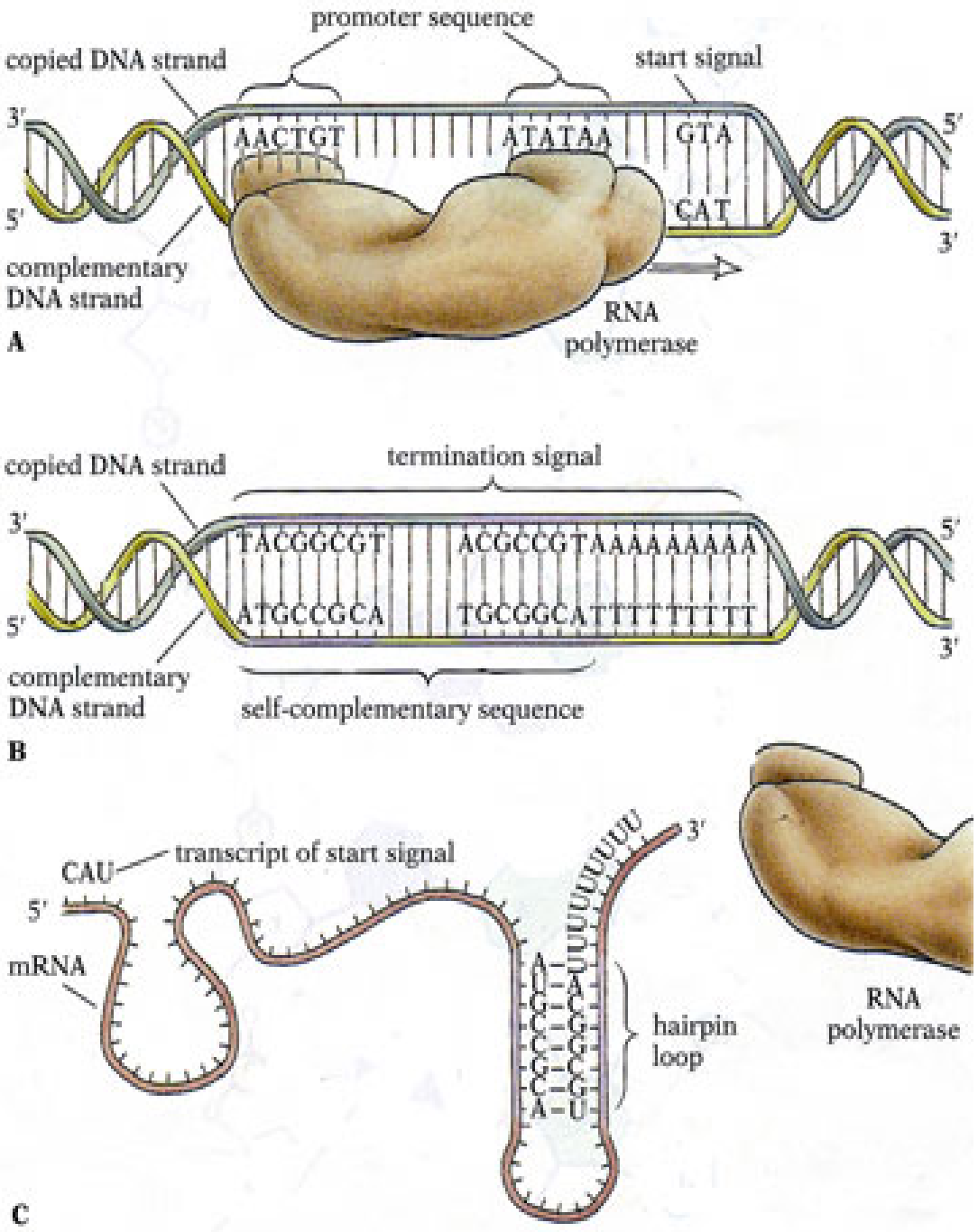
- Match RNA bases to DNA bases on one of the DNA strands
  - RNA pol II unwinds DNA 10-20 bases at a time
  - RNA pol II copies the information into RNA
    - RNA peels away from the template as the DNA bubble re-anneals behind the RNA polymerase





Termination: End of mRNA transcription

- Prokaryotes
  - RNA polymerase hits terminator sequence in DNA
    - mRNA forms hairpin loop by base pairing with itself at 3' end
      - RNA Pol. detaches from DNA
        - mRNA released



Termination: End of mRNA transcription

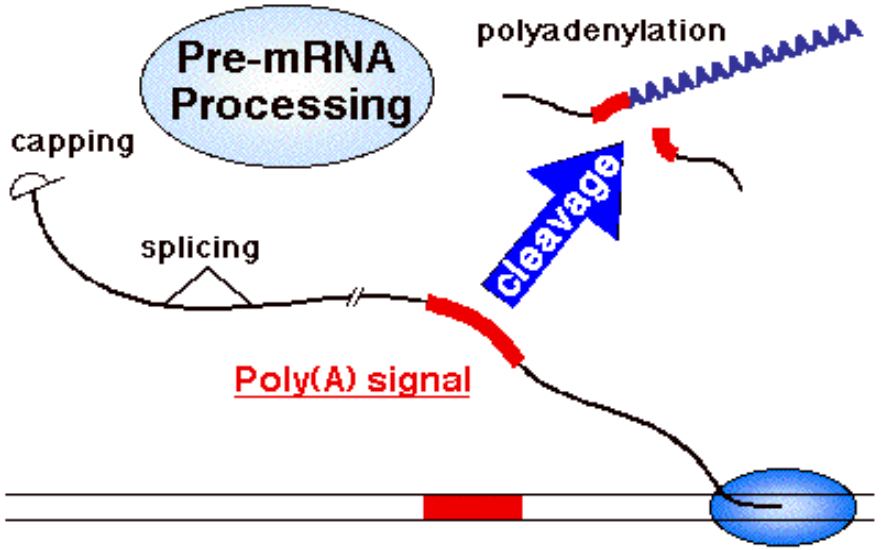
- Eukaryotes
  - RNA Pol II transcribes polyadenylation signal sequence
    - codes for AAUAAA in pre-mRNA
      - Special proteins "cut" the pre-mRNA free 10-35 nucleotides past this sequence
        - Polymerase continues transcribing DNA after this, but this transcript is degraded later and is not used

A Typical Poly A Signal

The Core SV40 early poly(A) signal

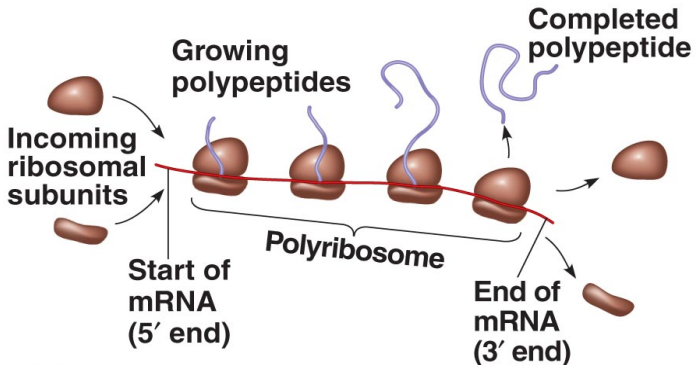
Cleavage

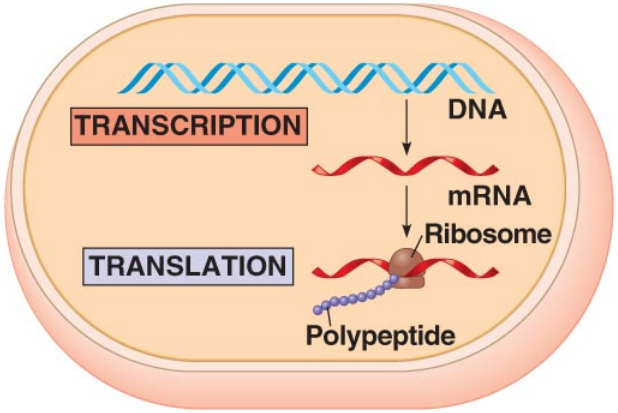
AATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGT



When genes that code for polypeptides are transcribed: Produce mRNA

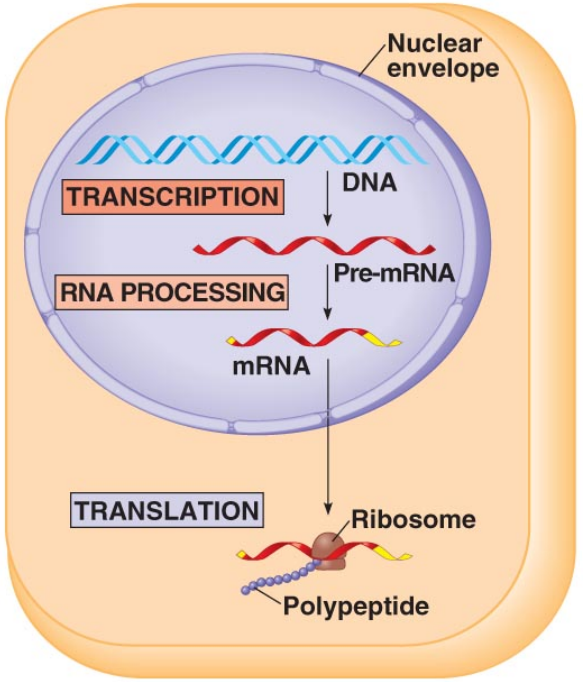
- In prokaryotes, this is made directly in the cytoplasm and starts being translated directly by ribosomes in the cytoplasm
  - Get: polyribosomes





(a) Bacterial cell

- What about in Eurkaryotes?
  - Transcription & translation are separated
  - AND before mRNA leaves the nucleus is undergoes is modified = RNA processing

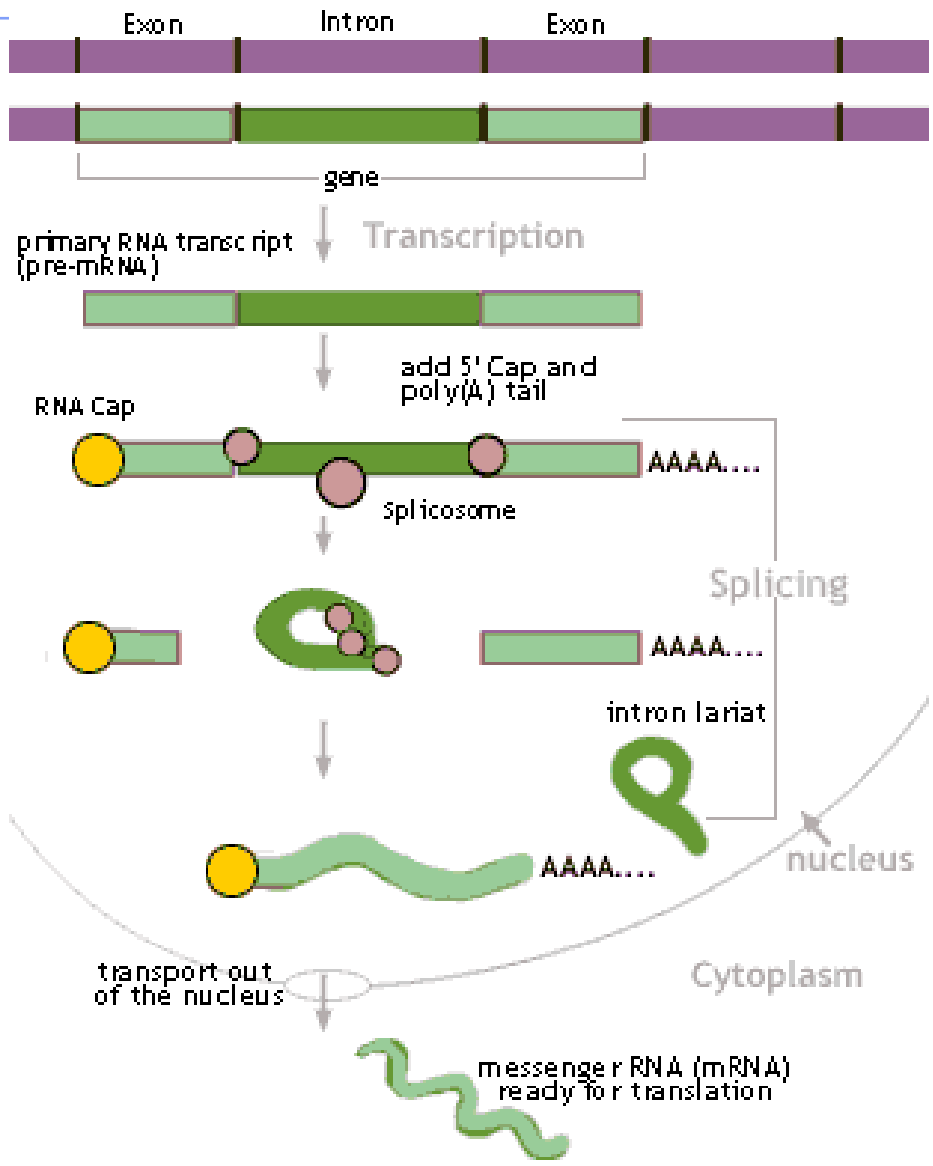


(b) Eukaryotic cell

RNA processing occurs in Eukaryotes

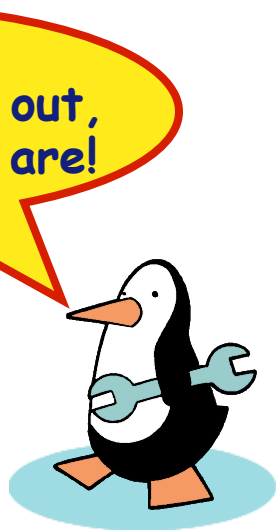
- **The modification of the primary transcript:**
  1. **RNA Splicing**
     - **Removal of Introns**
  2. **Alteration of the ends of the pre-mRNA**
     1) **Addition of the 5' Cap**
     2) **Addition of the Poly-A Tail**

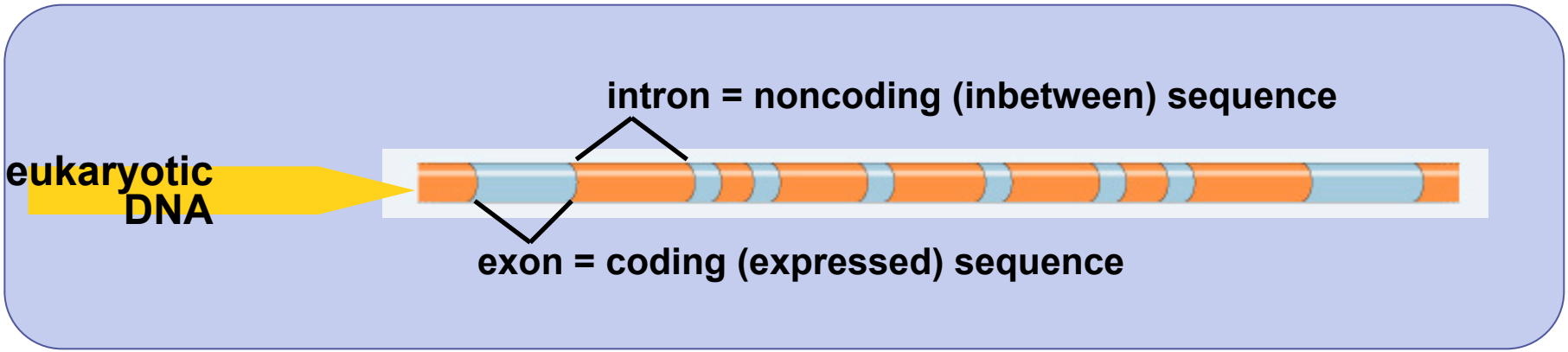
- **Pre-mRNA becomes mRNA**



Eukaryotic genes have 'junk'!

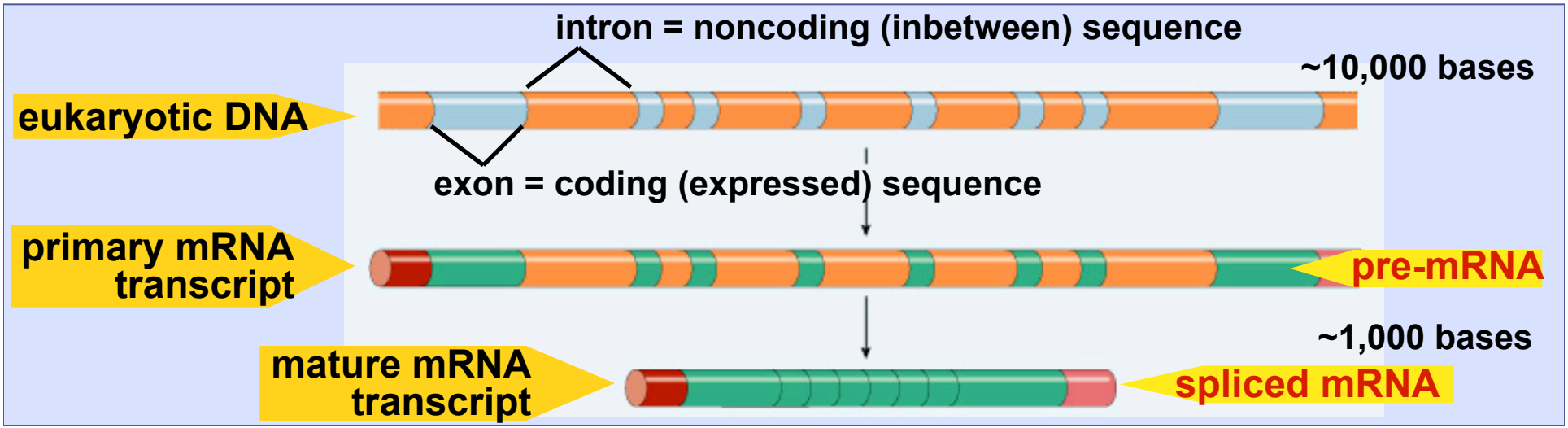
- Eukaryotic genes are not continuous
  - exons = the real gene
    - expressed / coding DNA
  - introns = the noncoding DNA
    - found in between coding sequence



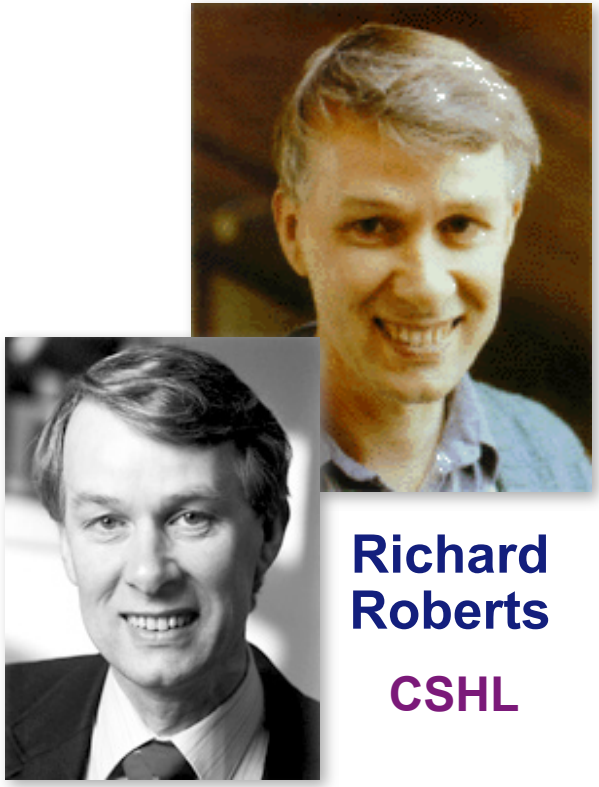


mRNA splicing

- ***Part of Post-transcriptional processing***
  - eukaryotic mRNA needs work after transcription
    - primary transcript = pre-mRNA
    - mRNA splicing
      - Cut out introns from the pre-mRNA and join the exons together
    - make mature mRNA transcript with a continuous
      - coding sequence



Discovery of exons/introns 1977 | 1993

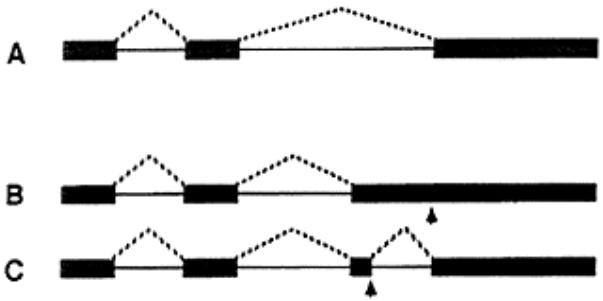


Richard Roberts

CSHL

Philip Sharp

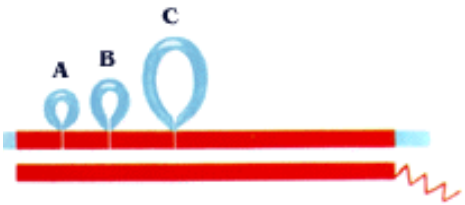
MIT



normal beta-globin gene

beta-thalassemia

inherited blood disorder that reduces the production of hemoglobin



Splicing must be accurate

- No room for mistakes!
  - a single base added or lost throws off the reading frame

AUGCGGCTATGGGUCCGAUAAGGGCCAU

AUGCGGUCCGAUAAGGGCCAU

AUG | CGG | UCC | GAU | AAG | GGC | CAU

Met | Arg | Ser | Asp | Lys | Gly | His

AUGCGGCTATGGGUCCGAUAAGGGCCAU

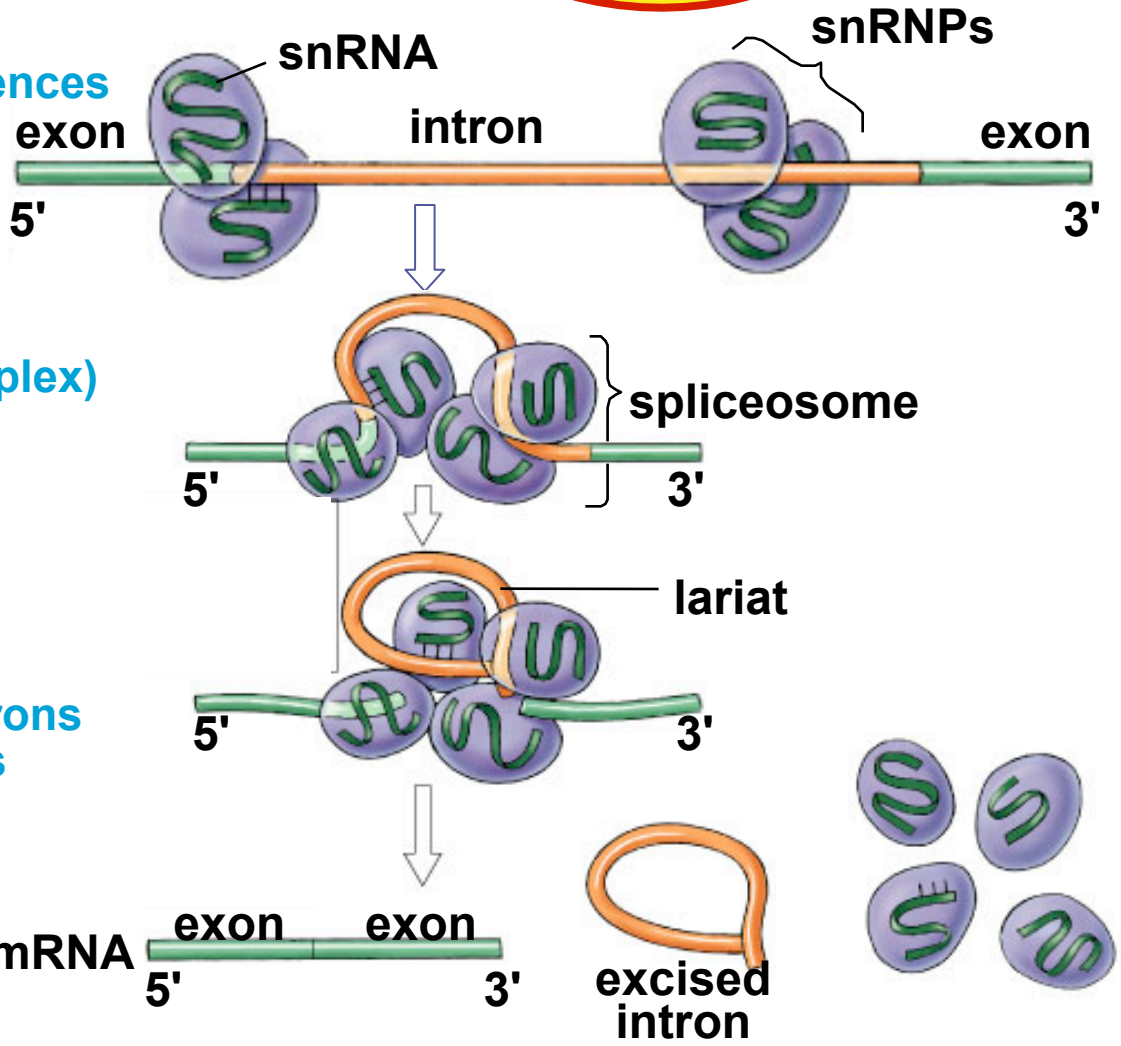
AUGCGGGUCCGAUAAGGGCCAU

AUG | CGG | GUC | CGA | UAA | GGG | CCA | U

Met | Arg | Val | Arg | STOP |

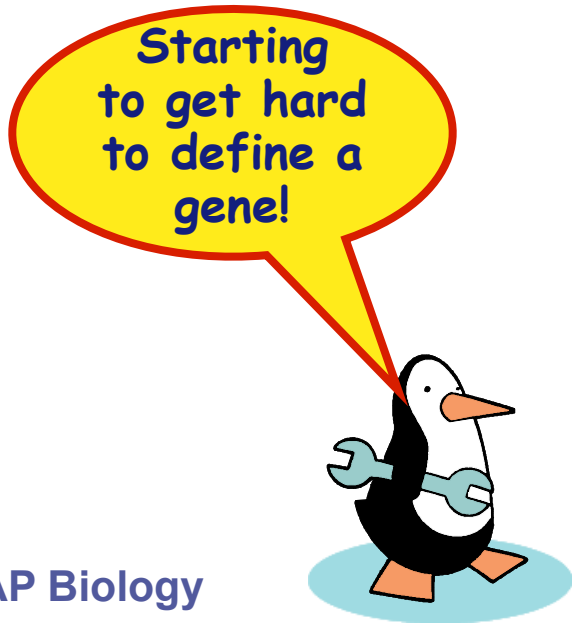
RNA splicing enzymes

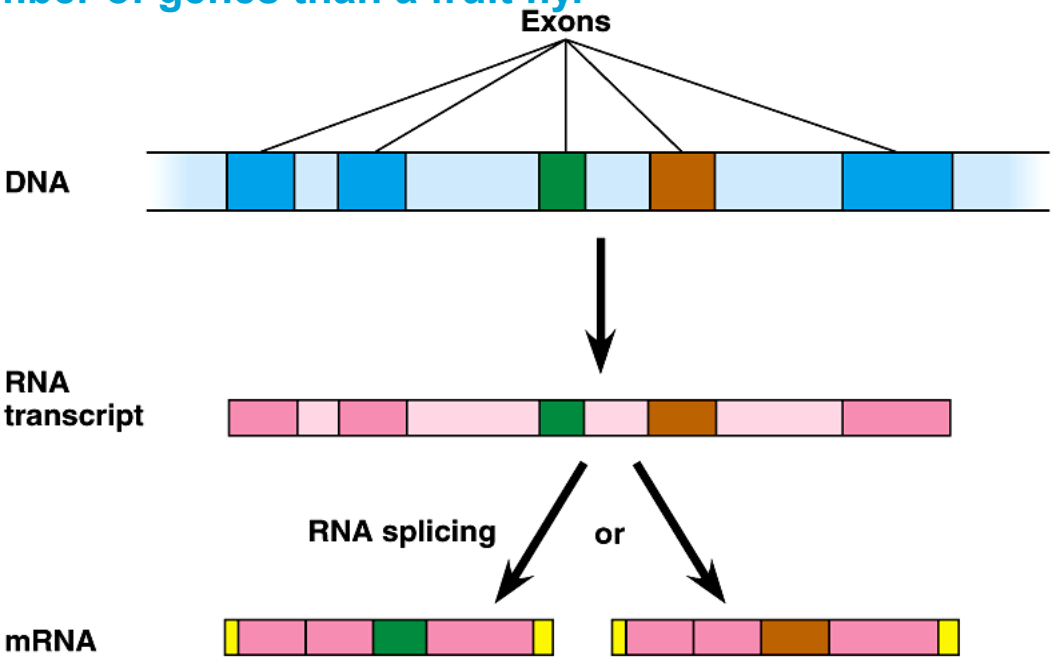
- **snRNPs** (= small nuclear riboproteins)
  - **Recognize spice sites**
    - Short nucleotide sequences at each end of introns
  - **Composition:**
    1. small nuclear RNA
    2. proteins
- **Spliceosome** (slicing complex)
  - **Composition:**
    1. several snRNPs
    2. Additional proteins
  - **Function:**
    - recognize splice site sequences, cut out introns & paste together exons



Alternative splicing

- One consequence of introns in genes is that one single gene can encode more than one kind of polypeptide
  - **Alternative Splicing**: Allows for the production of alternative mRNAs from SAME gene
    - Different segments of pre-mRNA can be treated in many genes as exons or introns during RNA processing.
      - Ex: reason humans can be so complex with only half the number of genes than a fruit fly.



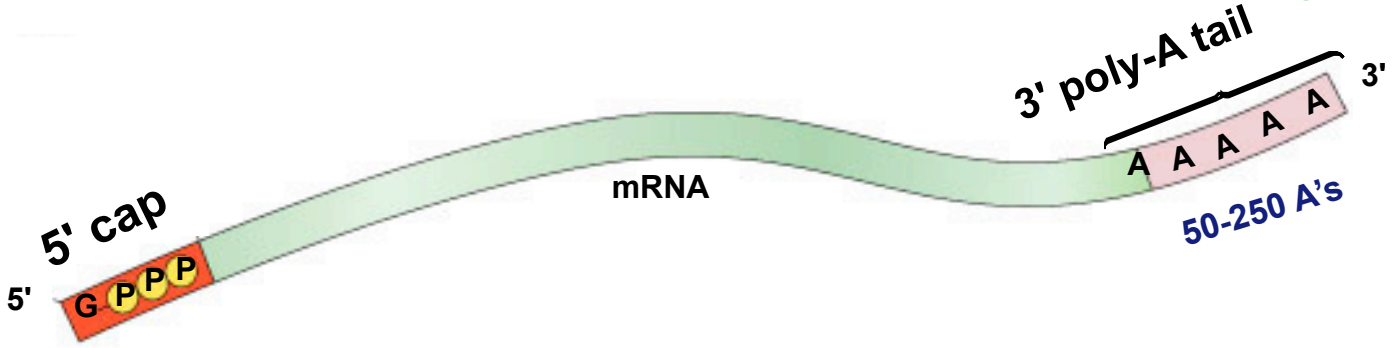


More post-transcriptional modifications

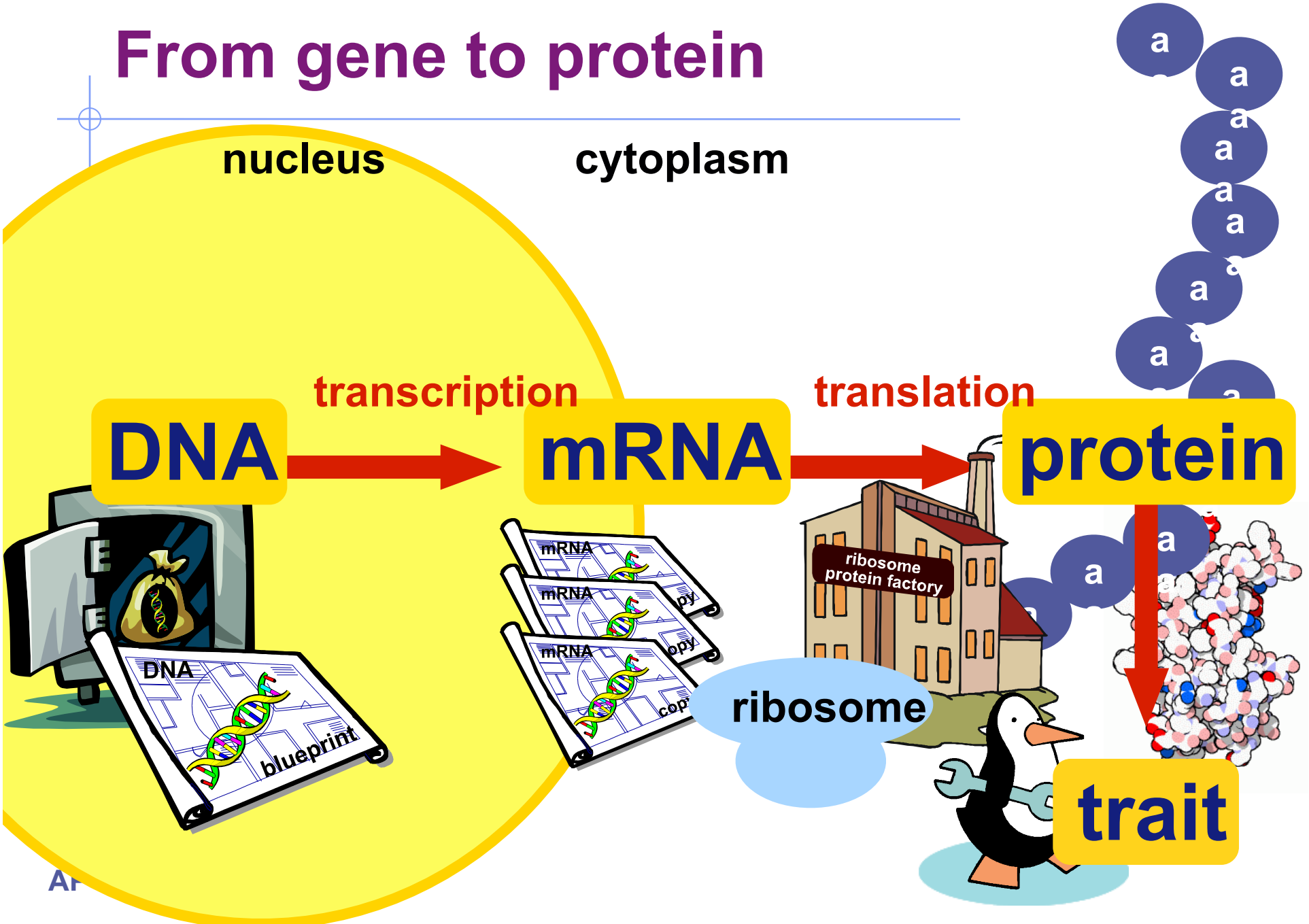
- Add 5′ GTP Cap
- Enzyme adds poly-A tail (50-250 A nucleotides)

Functions:

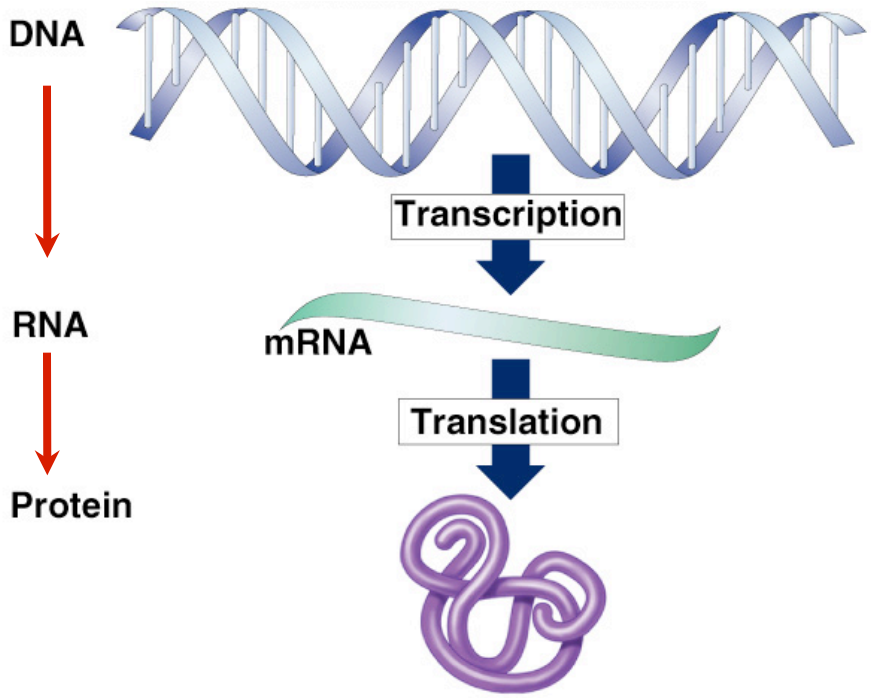
1. The longer tail, the longer mRNA lasts
   - Results in the production of more protein
2. Hydrolytic enzymes in cytoplasm attack mRNA
   - Modifications protect the ends of the molecule from degradation
3. Help export mRNA from nucleus
4. Help ribosomes attach to the 5' end of mRNA in cytoplasm



From gene to protein



Translation



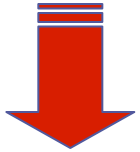
Translating the nucleic acid language to the amino acid language

How does mRNA code for proteins?

DNA

4 ATCG

TACGCACATTTACGTACGCGG



mRNA

4 AUCG

AUGCGUGUAAAUGCAUGCGCC

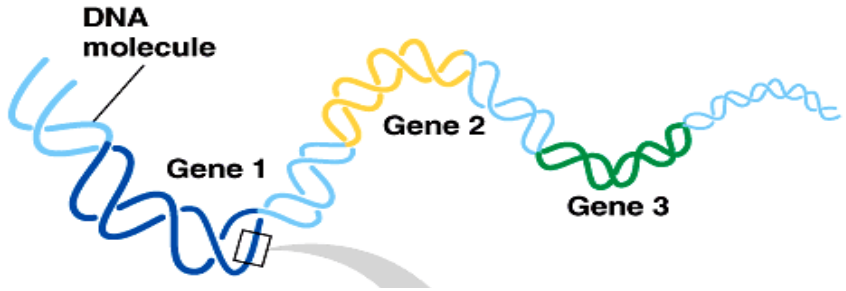
protein

20

Met Arg Val Asn Ala Cys Ala

How can you code for 20 amino acids with only 4 nucleotide bases (A,U,G,C)?

mRNA codes for proteins in NON-overlapping triplets of nucleotides



DNA

TACGCACATTTACGTACGCGG

codon

mRNA

AUGCGUGUAAAUGCAUGCGCC

protein

Met Arg Val Asn Ala Cys Ala

Cracking the code

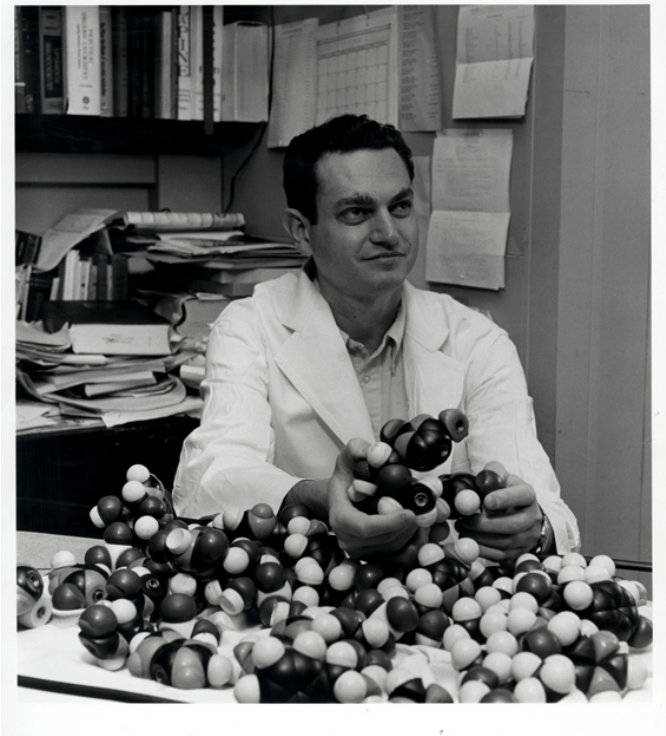
1960 | 1968
Nirenberg & Khorana

- **Crick**
  - if 1 nucleotide codes 1 amino acid = code only 4 types of amino acids
  - if 2 nucleotides code 1 amino acid = code only 4^2 (16) amino acids
  - if 4 nucleotides code 1 amino acid = code 4^4 (256) amino acids
  - hypothesized 3-letter (triplet) codon system (64)

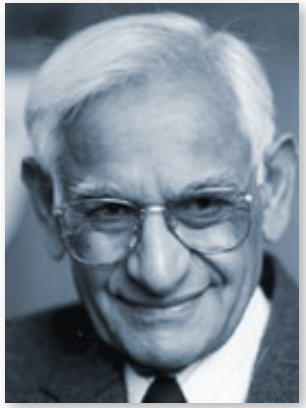
WHYDIDTHEREDBATEATTHEFATRAT

- **Nirenberg & Khorana**
  - Cracked the code
    - determined mRNA–amino acid match
  - added (synthetic) fabricated mRNA to test tube of ribosomes, tRNA & amino acids
    - created artificial UUUUU… mRNA
    - found that UUU coded for phenylalanine

Marshall Nirenberg



1960 | 1968



Har Khorana

AP

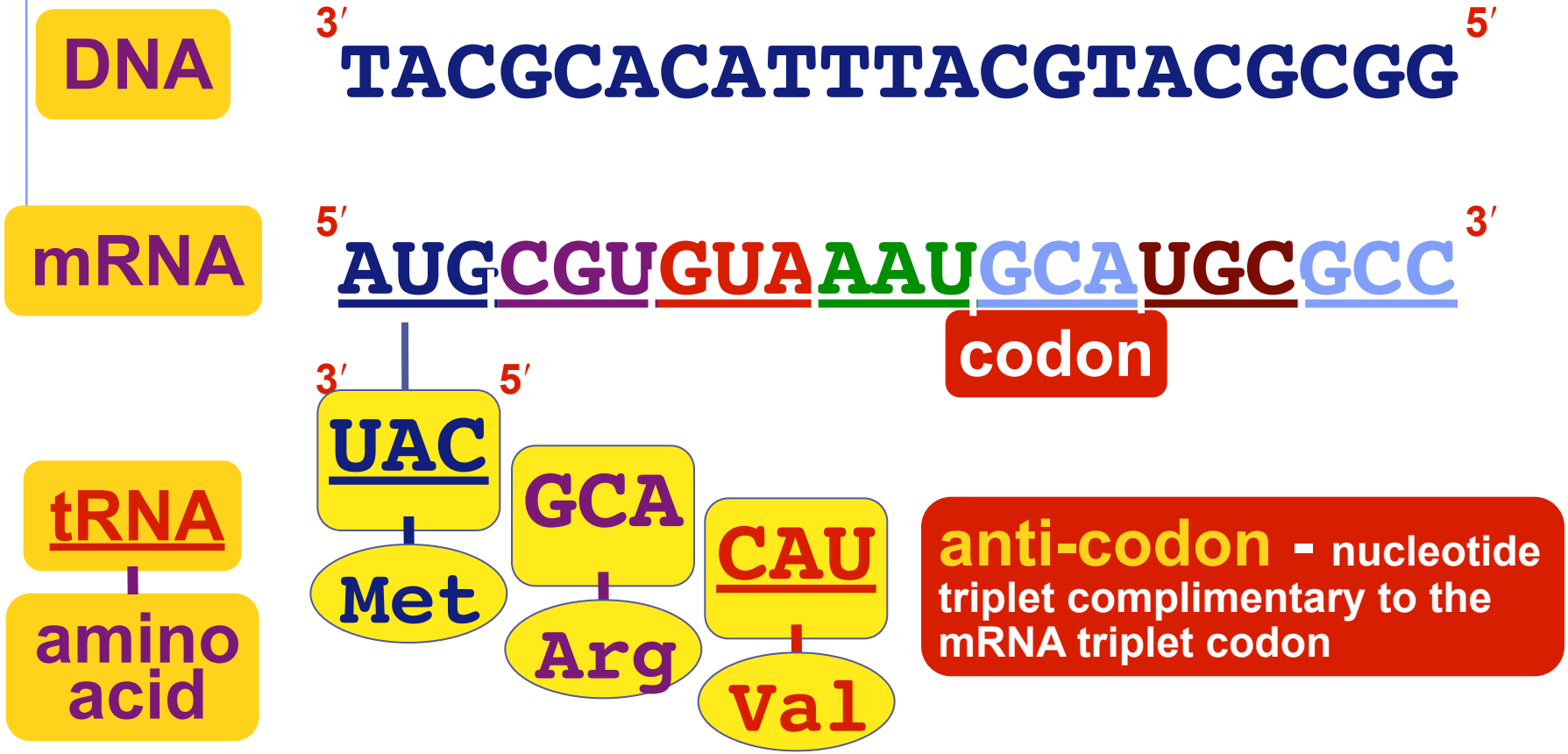
The code

- **Universal genetic code for almost ALL life!**
  - strongest support for a common origin for all life
- **Code is redundant but NOT ambiguous**
  - several codons for each amino acid
  - 3rd base "wobble"

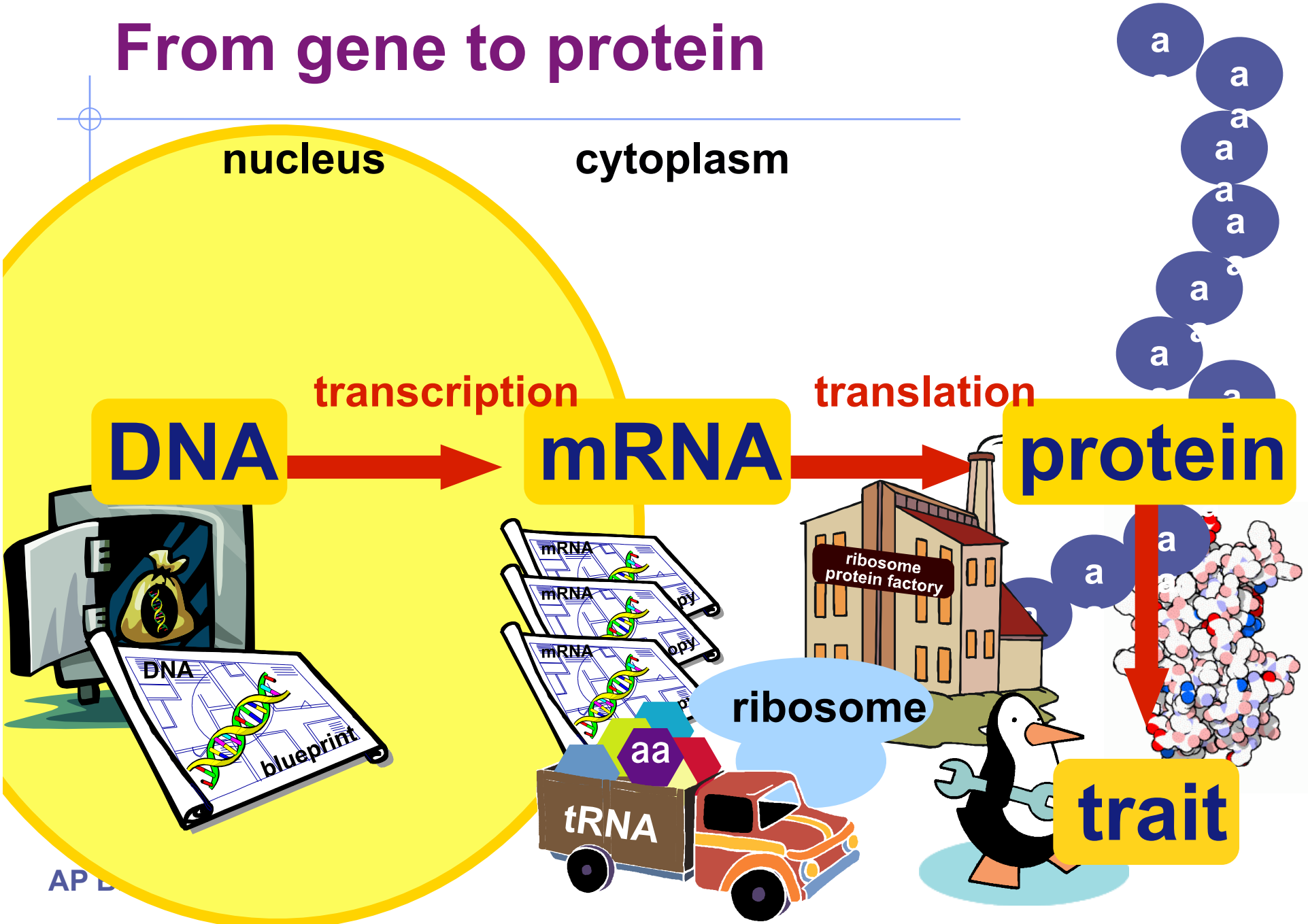
- **Start codon**
  - **AUG**
    - Codes for a.a. methionine
- **Stop codons**
  - **UGA, UAA, UAG**
    - Do not code for an amino acid

First base (5′ end)	Second base: U	Second base: C	Second base: A	Second base: G	Third base (3′ end)
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 or start	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

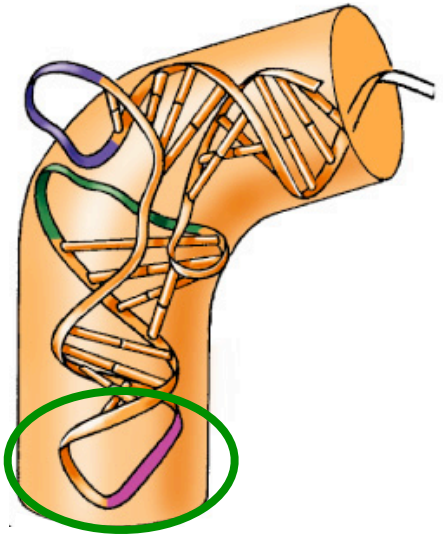
How are the codons matched to amino acids?



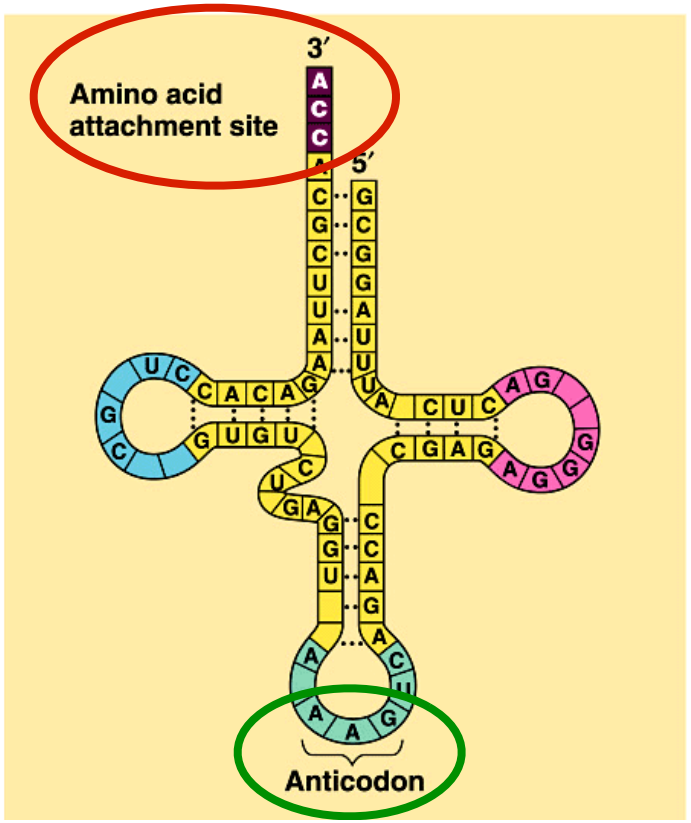
From gene to protein

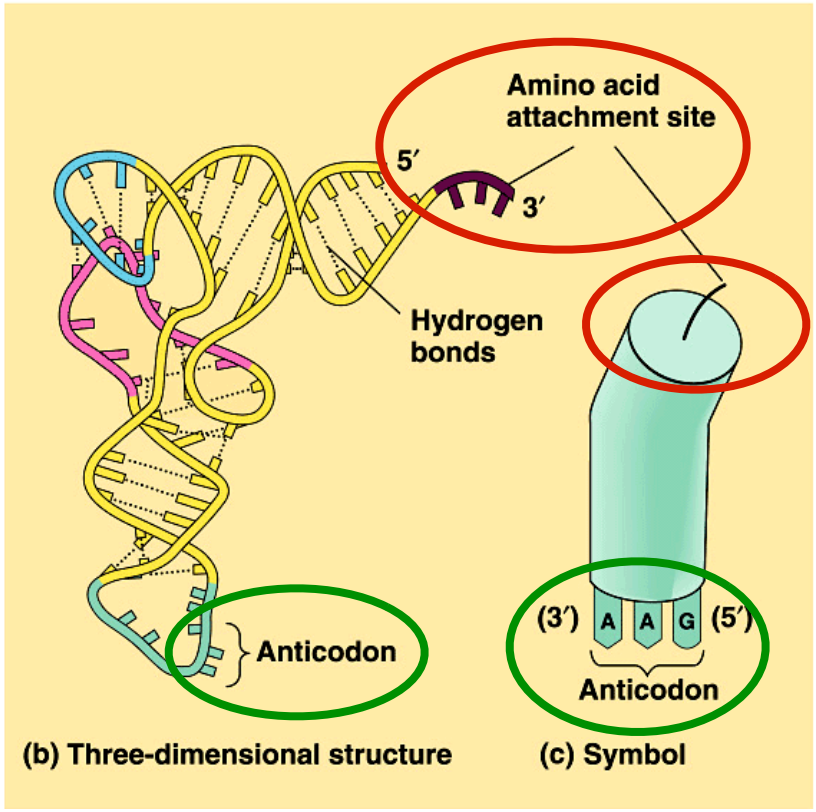


Transfer RNA structure



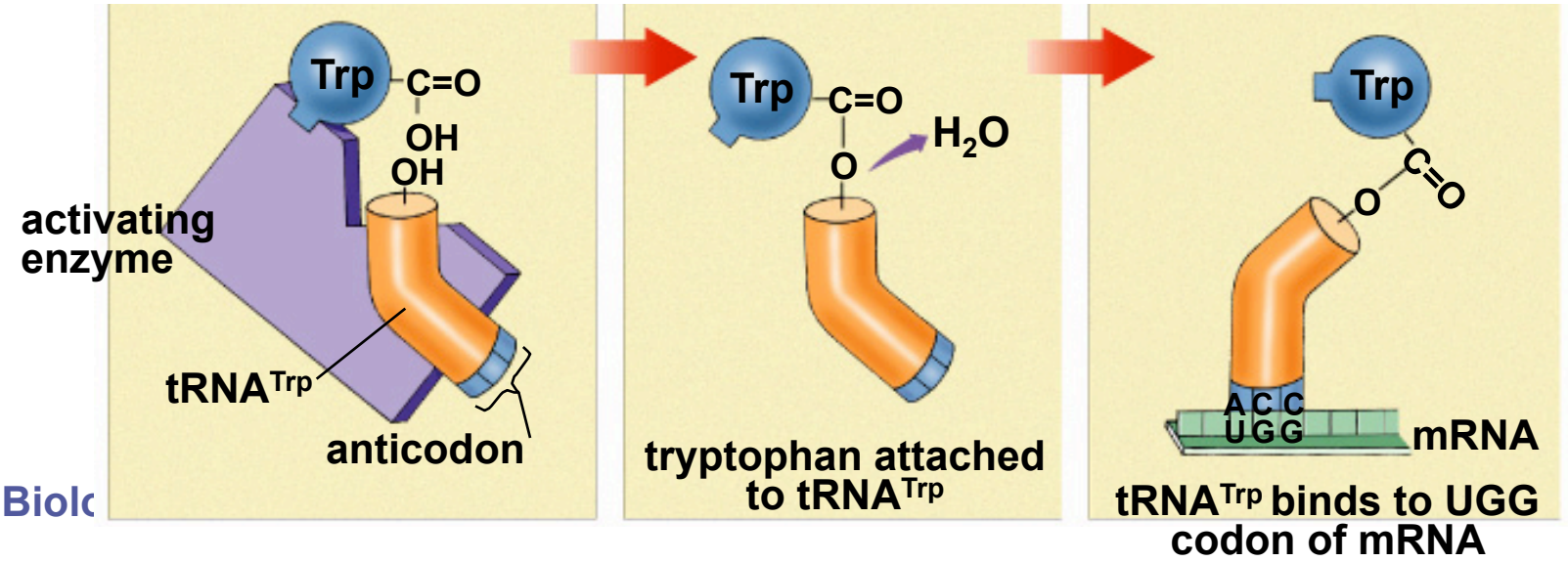
- "Clover leaf" structure
  - Held together by base paring within one single stranded tRNA molecule
  - anticodon on "clover leaf" end
  - amino acid attached on 3′ end



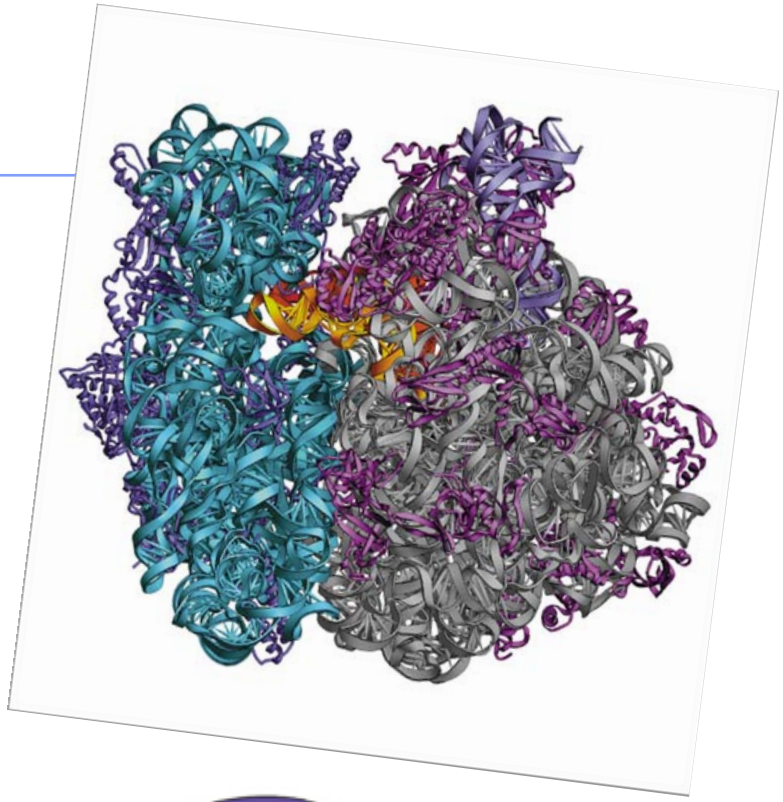


Loading tRNA

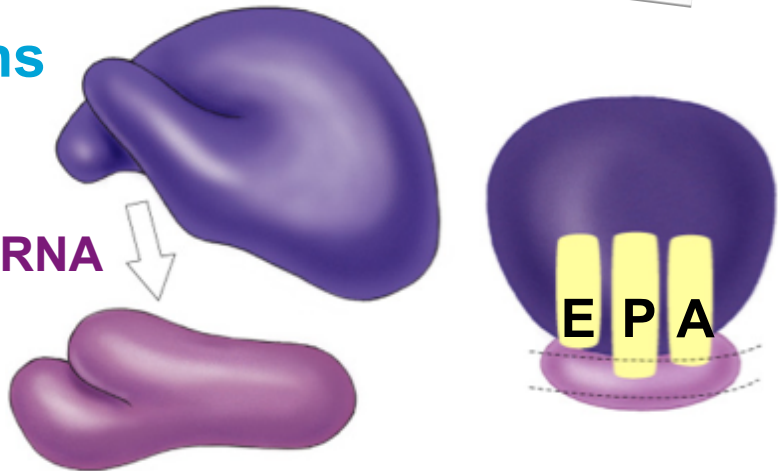
- **Aminoacyl tRNA synthetase**
  - enzyme which bonds amino acid to tRNA
    - 20 different types on for each amino acid
    - Each one bonds all the tRNA's that are able to code for that amino acid
  - Creating the bond requires energy
    - ATP → AMP + Energy
    - covalent bond between the tRNA and Amino Acid is unstable
      - so it can release amino acid at ribosome easily



Ribosomes

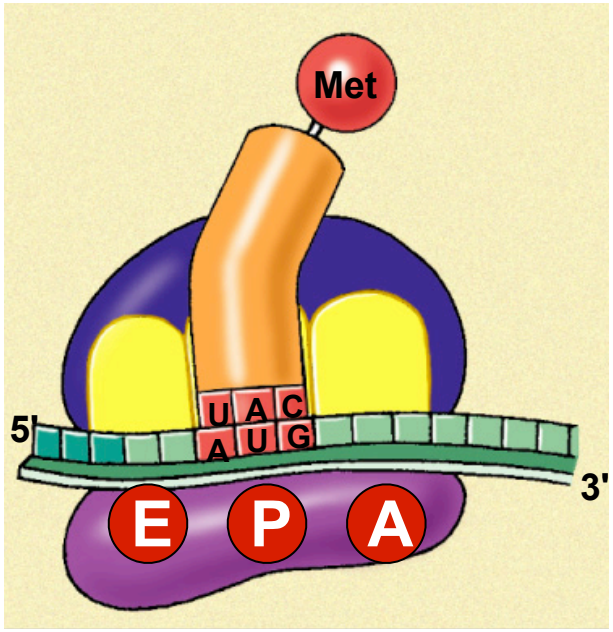


- Facilitate coupling of tRNA anticodon to mRNA codon and catalyze the construction of a polypeptide chain
  - organelle or enzyme? Neither!
  - rRNA's - not proteins - act as catalysts
- Structure
  - ribosomal RNA (rRNA) & proteins
  - 2 subunits
    - Large
      - Contains the binding sites for tRNA
      - where amino acids added to growing polypeptide chain
    - Small
      - Contains mRNA binding site



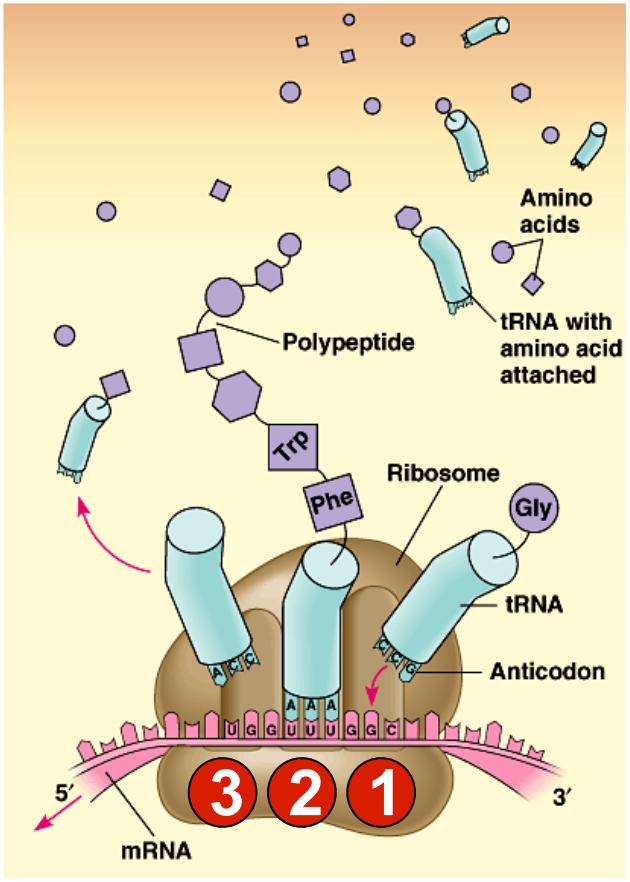
Ribosomes

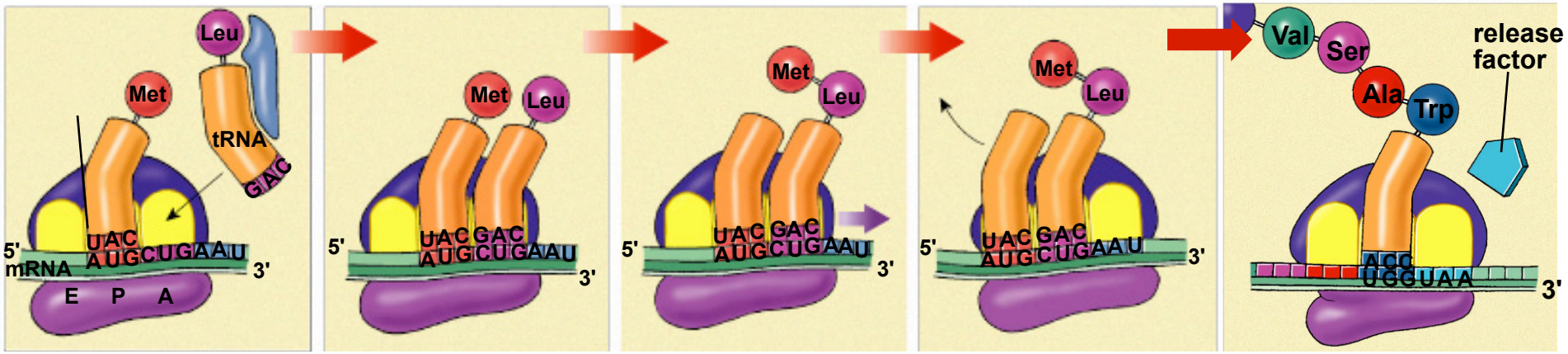
- A site (aminoacyl-tRNA site)
  - holds tRNA carrying next amino acid to be added to chain
- P site (peptidyl-tRNA site)
  - holds tRNA carrying growing polypeptide chain
- E site (exit site)
  - empty tRNA leaves ribosome from exit site



Building a polypeptide

1. **Initiation**
   - brings together mRNA, ribosome subunits, initiator tRNA
2. **Elongation**
   - adding amino acids to the growing polypeptide
   - tRNA's recognize and bind mRNA codon sequence
3. **Termination**
   - Occurs when mRNA presents a stop codon
   - Release factor enters A site

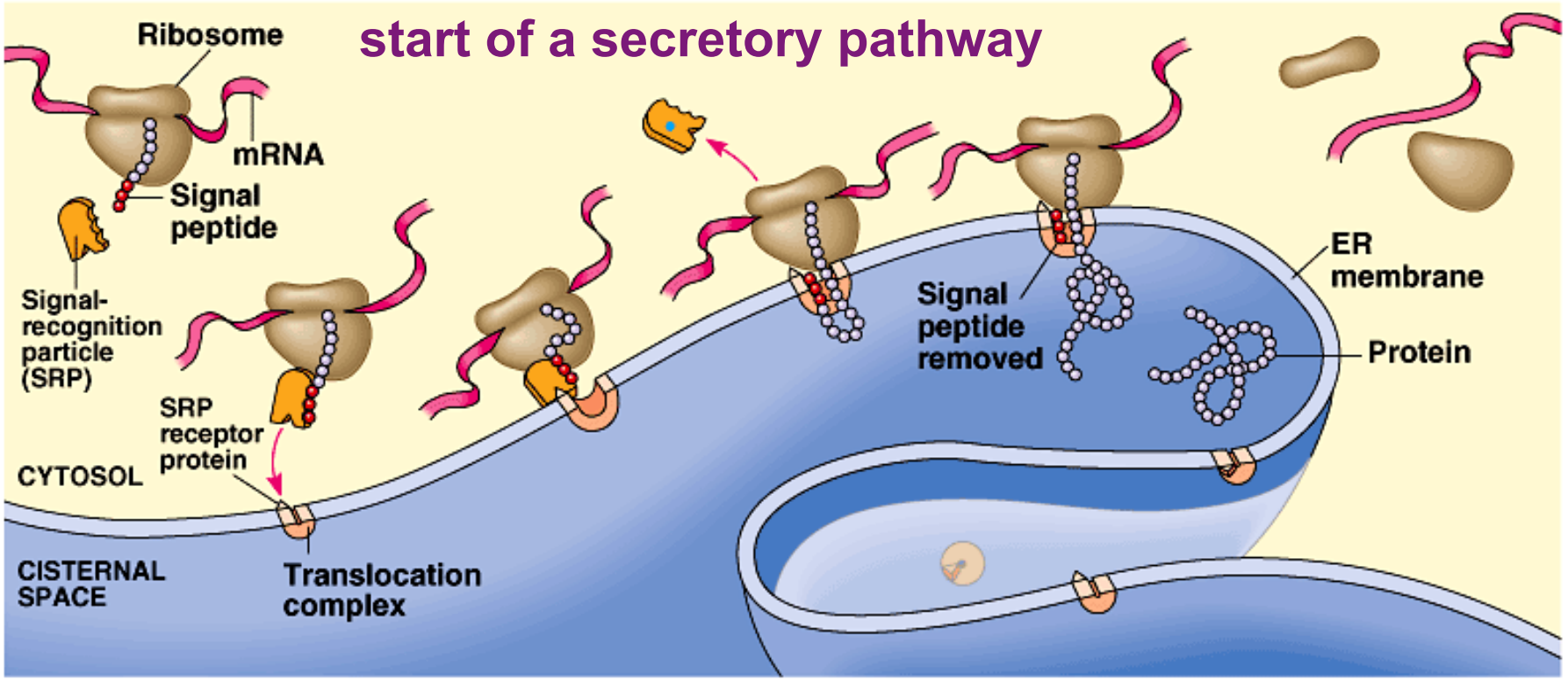




“Protein targeting”

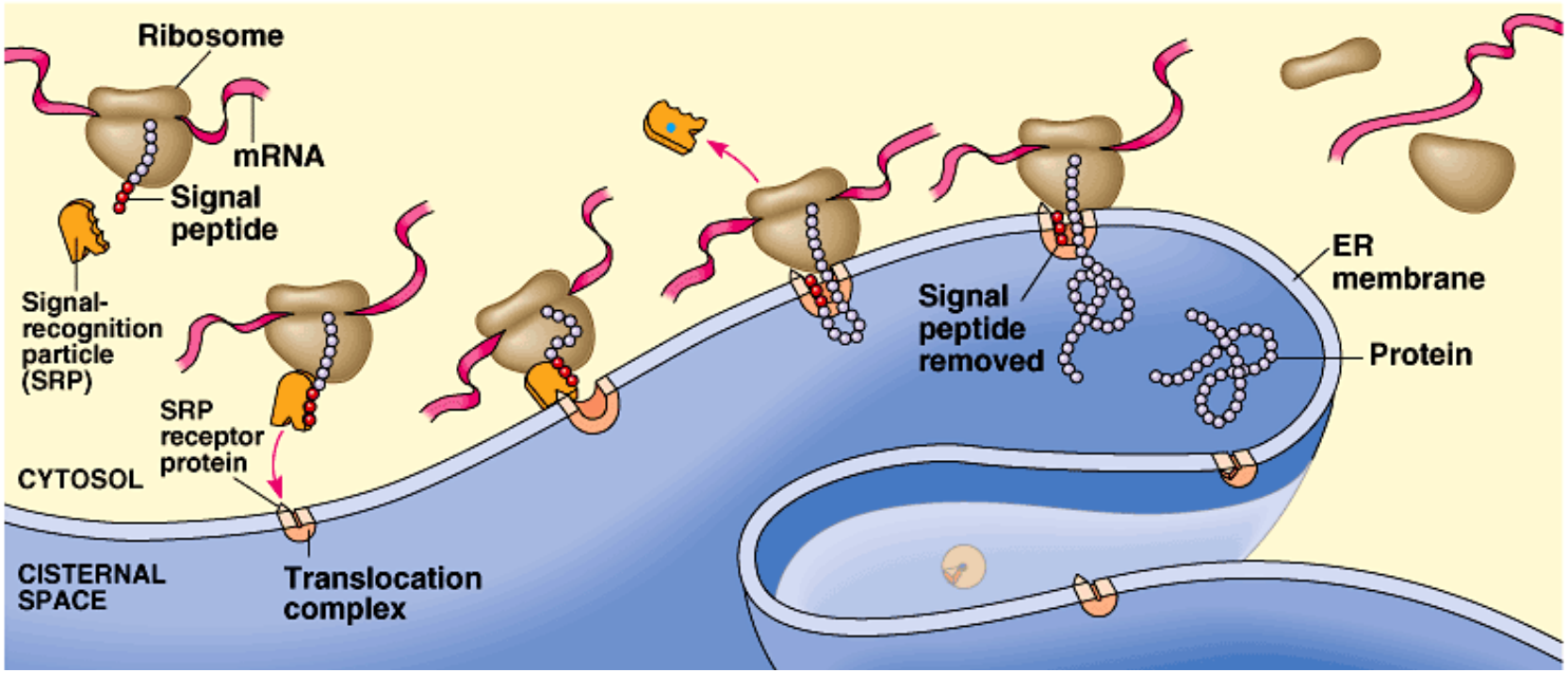
- Free ribosomes synthesize proteins that will stay in the cytosol
- Bound ribosomes make proteins of the endomembrane system and secreted proteins

- All ribosomes are identical and all proteins start off being synthesized on FREE ribosomes



“Protein targeting”

- **How do proteins get fed into the RER?**
  - Growing polypeptide is marked by a Signal peptide (‘address label’)
    - Sequence of 20 amino acids at the leading end (N-terminus) of the polypeptide
  - Recognized by Signal-Recognition Particle (SRP)
    - Brings ribosome to a receptor in the ER membrane
  - Growing polypeptide is snaked through protein pore into ER lumen or remains partially embedded in the ER membrane



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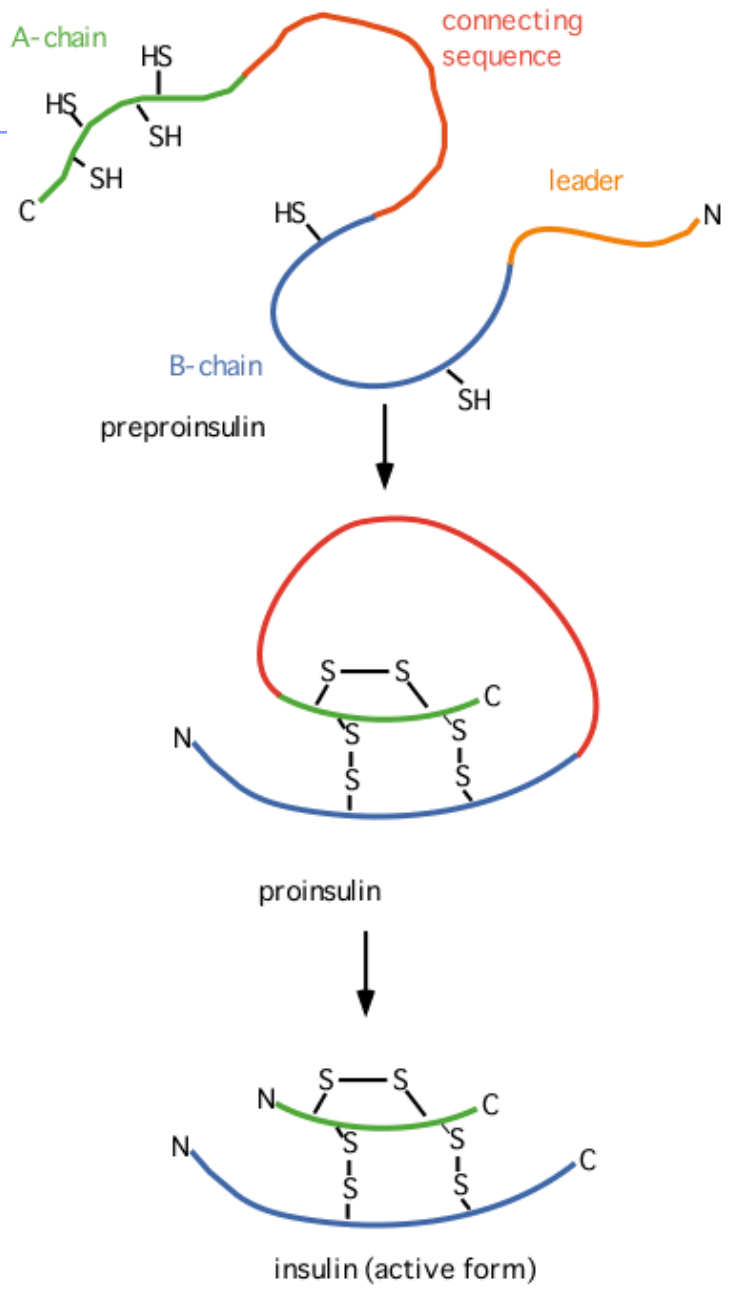
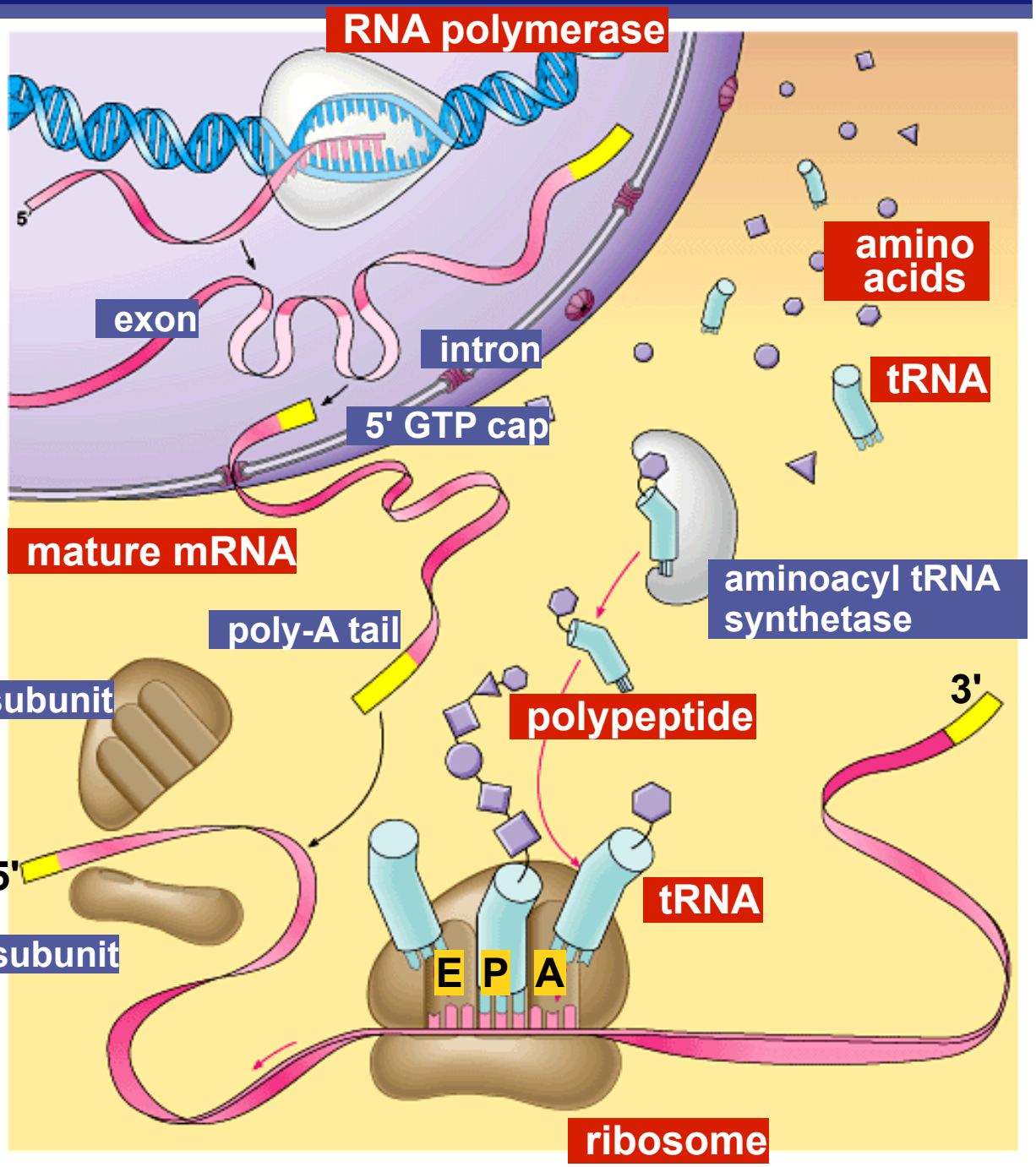
Post-translation

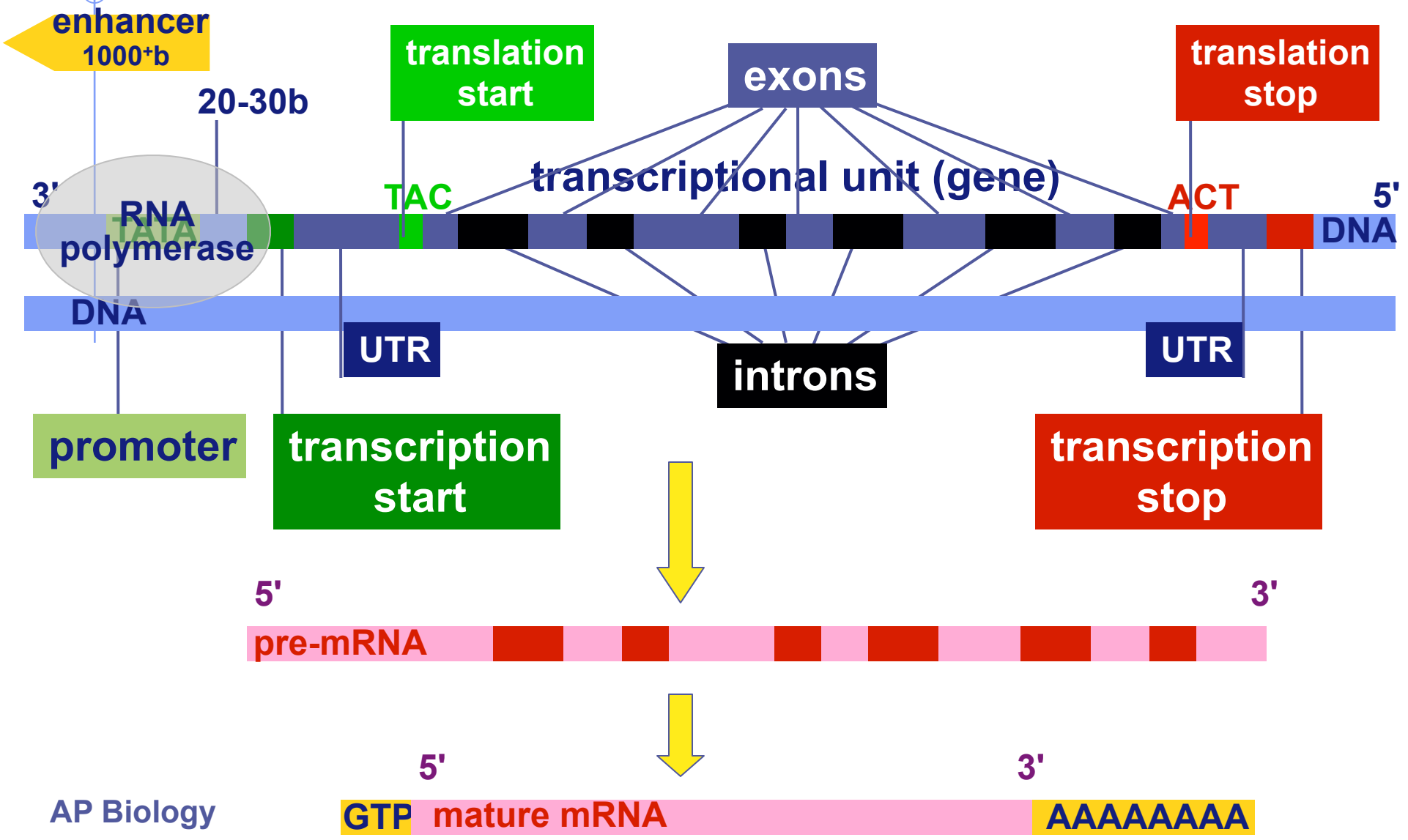
- **Proteins undergo *Protein folding & Post-Translational Modification:***
  - **Amino acids may be chemically modified:**
    1. **Attach sugars, lipids, phosphates etc..**
    2. **Amino acids may be removed from the beginning of the polypeptide**
    3. **Polypeptide may be cleaved in 2 or more pieces**
    4. **Quaternary structure takes shape**



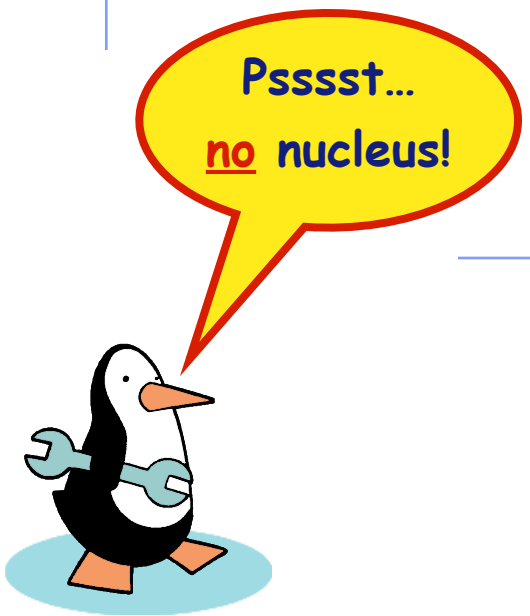
Can you tell the story?

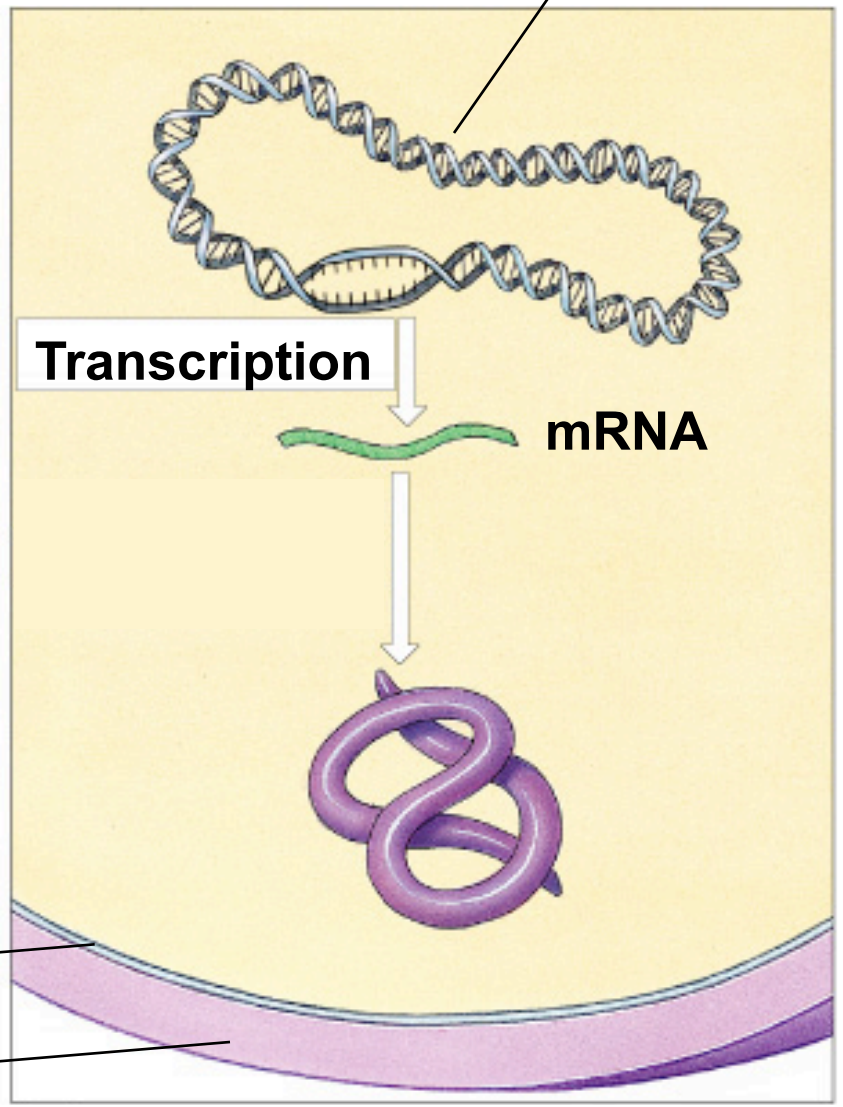


The Transcriptional unit (part of the gene)



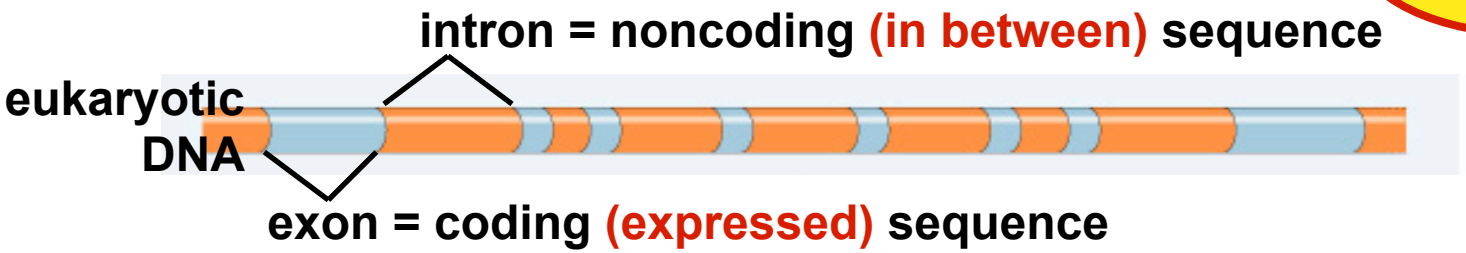
Protein Synthesis in Prokaryotes

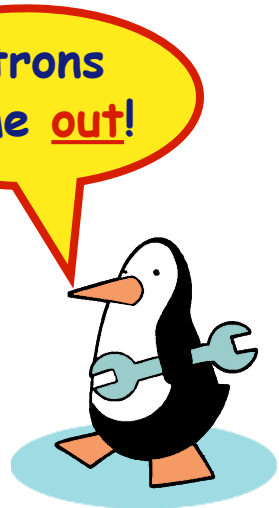




Prokaryote vs. Eukaryote genes

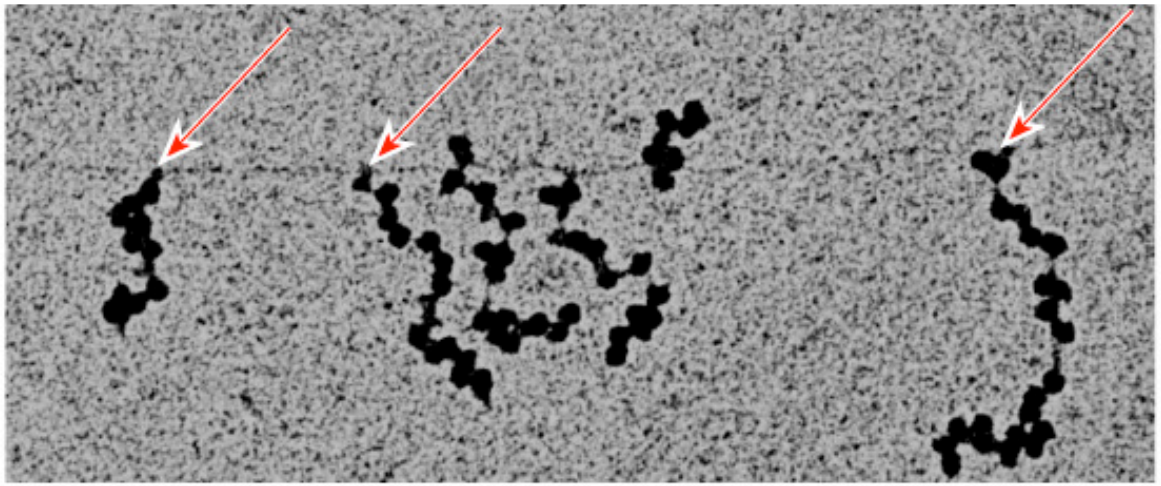
- **Prokaryotes**
  - DNA in cytoplasm
  - circular chromosome
  - naked DNA
  - NO introns
- **Eukaryotes**
  - DNA in nucleus
  - linear chromosomes
  - DNA wound on histone proteins
  - introns vs. exons

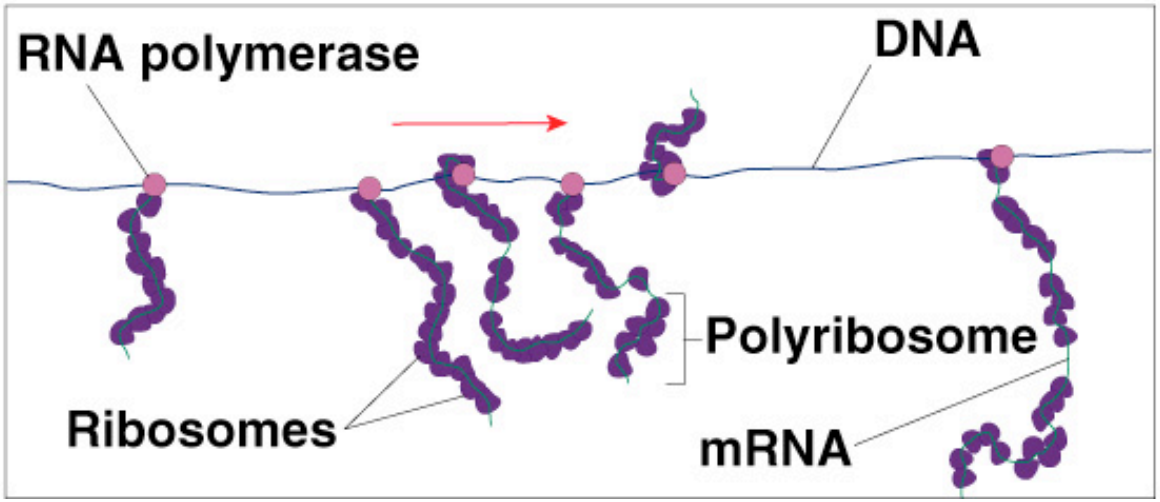




Translation in Prokaryotes

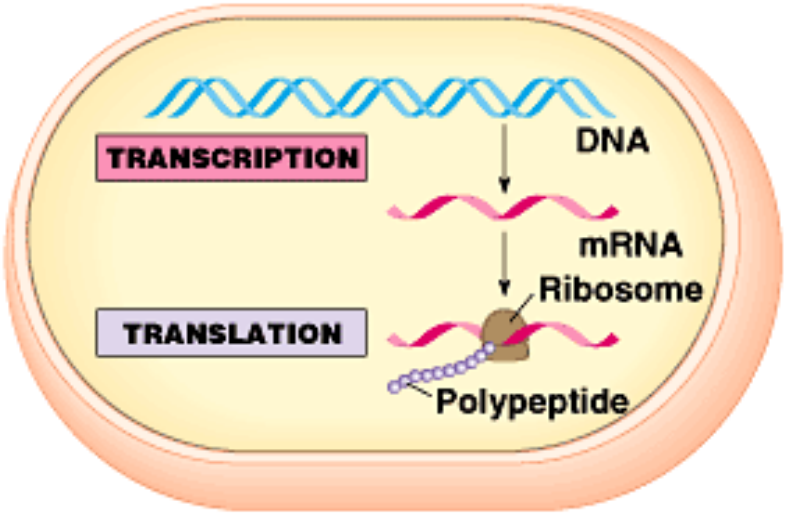
- **Transcription & translation are simultaneous in bacteria**
  - DNA is in cytoplasm
  - no mRNA editing
  - ribosomes read mRNA as it is being transcribed



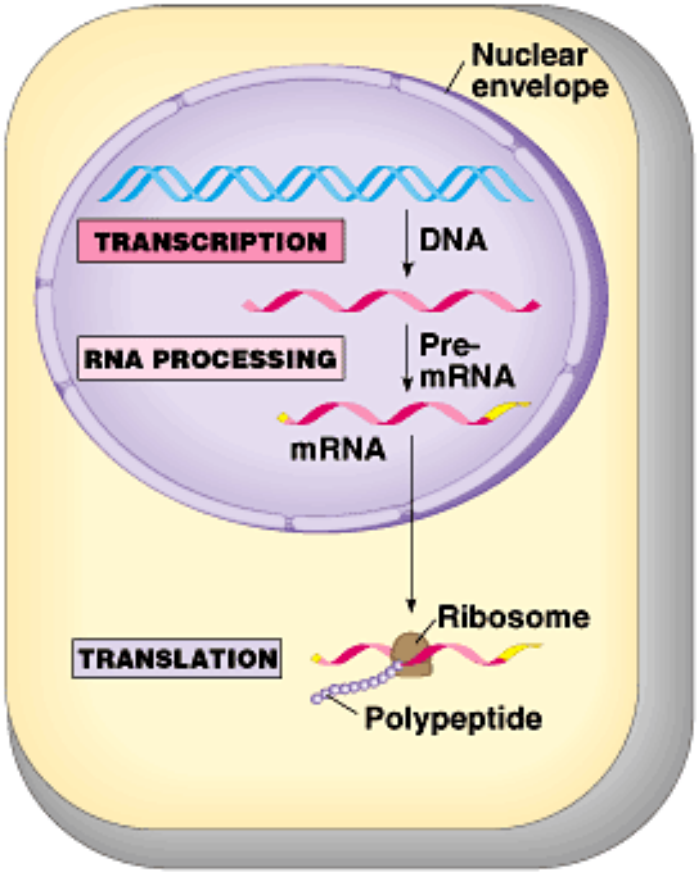


Translation: prokaryotes vs. eukaryotes

- **Differences between prokaryotes & eukaryotes**
  - **time & physical separation between processes**
    - **takes eukaryote ~1 hour from DNA to protein**
  - **no RNA processing in prokaryotes**



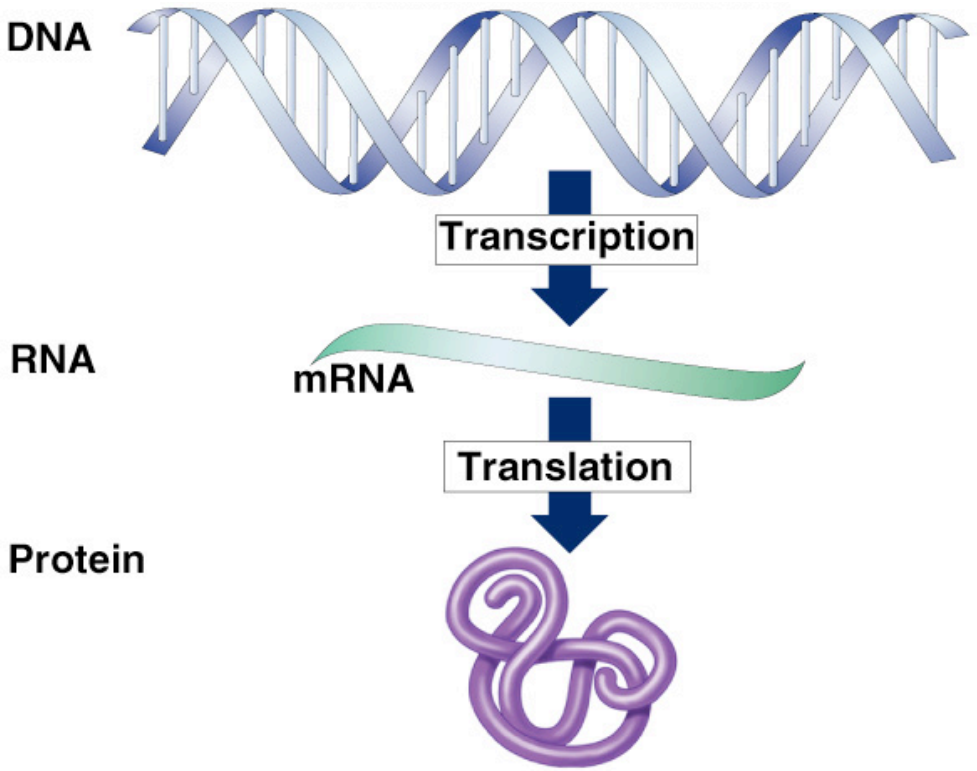
(a) Prokaryotic cell



(b) Eukaryotic cell

Any Questions??

What color would a smurf turn if he held his breath?



DNA Mutations

(b) Sickled red blood cells and the primary structure of sickle-cell hemoglobin

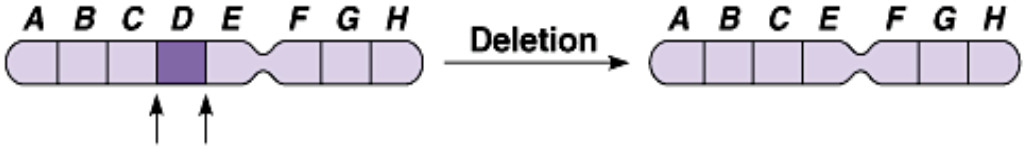
Types of Mutations

- **Mutations = Changes in DNA**
  - Changes in DNA may cause a cell to not be able to made specific RNA molecules or proteins
    - Changes in DNA may cause a cell to make RNA molecules and proteins that have an altered shape and, therefore, different function or lack of function
      - PROTEIN SHAPE = FUNCTION
- Mutations can happen on a large or small scale
  - Gross Chromosomal Mutations involve changes to large sections of a chromosome
    - *Involves the entire gene or many genes*
  - Point Mutations involve changes to one or a few nucleotides or base pairs
    - *Involves just one loci in the DNA or just one gene*

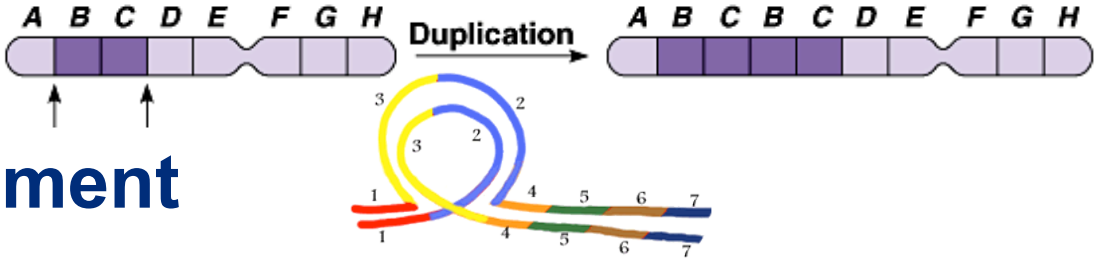
Large-scale mutations - Large changes in chromosome structure involving

error of replication

- **deletion**
  - loss of a chromosomal segment



- **duplication**
  - repeat a segment

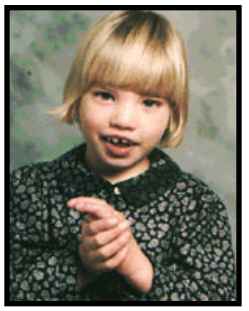


error of crossing over

- **inversion**
  - reverses a segment

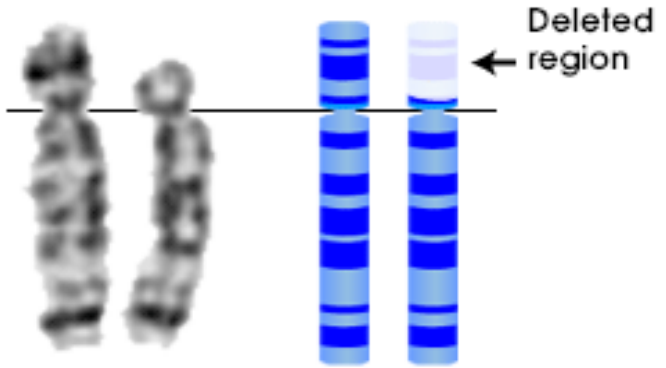
- **translocation**
  - move segment from one chromosome to another

Cri-du-Chat Syndrome

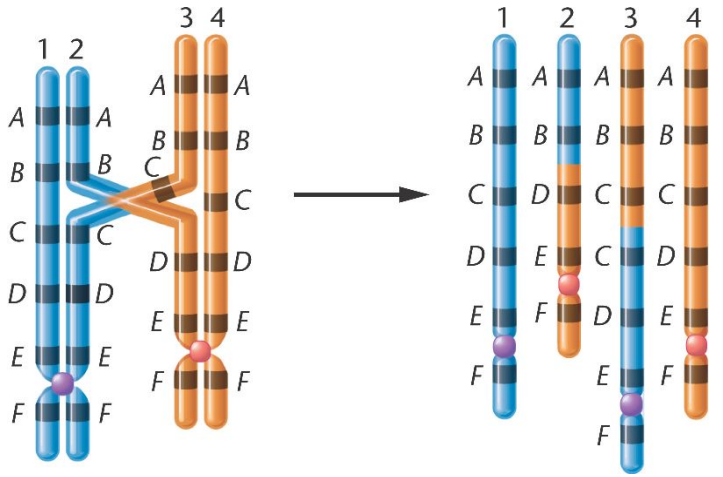


Caused by a chromosomal deletion.

- Deletion may result because of unequal recombination during meiosis when forming egg or sperm.
  - Babies are small at birth & may have respiratory problems along with distinct phenotypic features.
    - Often, the larynx doesn't develop correctly, which causes the signature cat-like cry.
    - They have a small head [microcephaly], round face, small chin, wide set eyes, folds of skin over eyes, small bridge of nose
    - May have heart defects, muscular or skeletal problems, hearing or sight problems, or poor muscle tone.
    - Difficulty walking and talking correctly.
    - Behavior problems (such as hyperactivity or aggression)
    - Severe mental retardation.



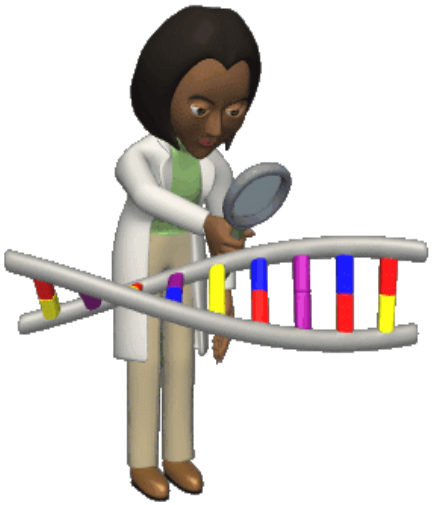
Cri-du-chat Chromosome 5 pair

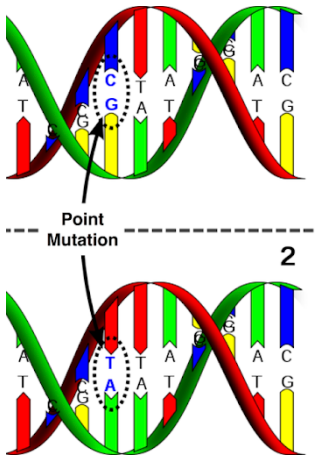


Unequal Crossing Over

Small-scale Mutations

- **Mutations** are responsible for the diversity of genes found among organisms
  - They are the ultimate source of new alleles and genes
- **Point mutations**
  - single or small base changes in a gene or specific locus of DNA
    - **Two types**:
      1. Base-pair Substitutions
      2. Base-Pair Insertions or Deletions



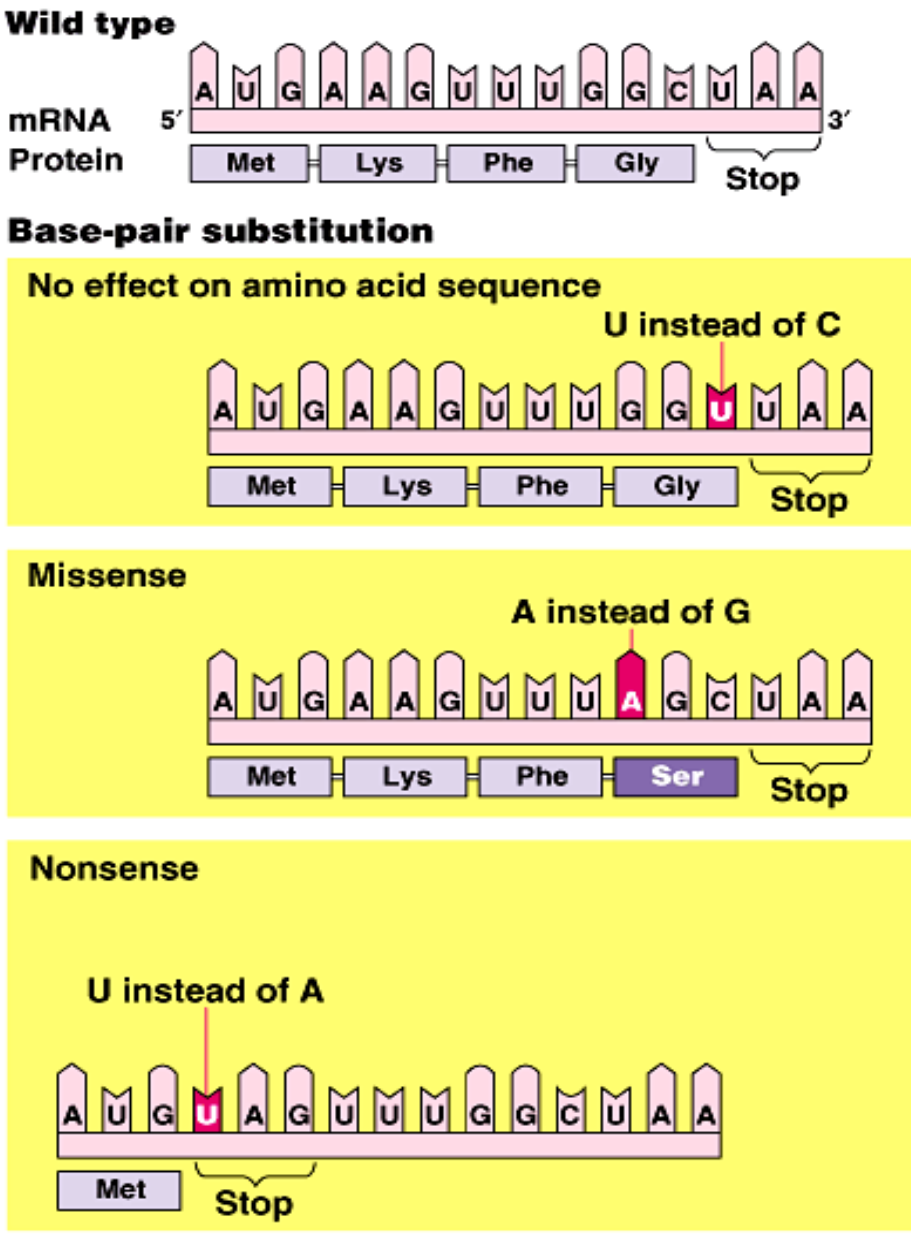


When do mutations affect the next generation?

When mutation takes place in a gamete or in a cell that produces gametes.

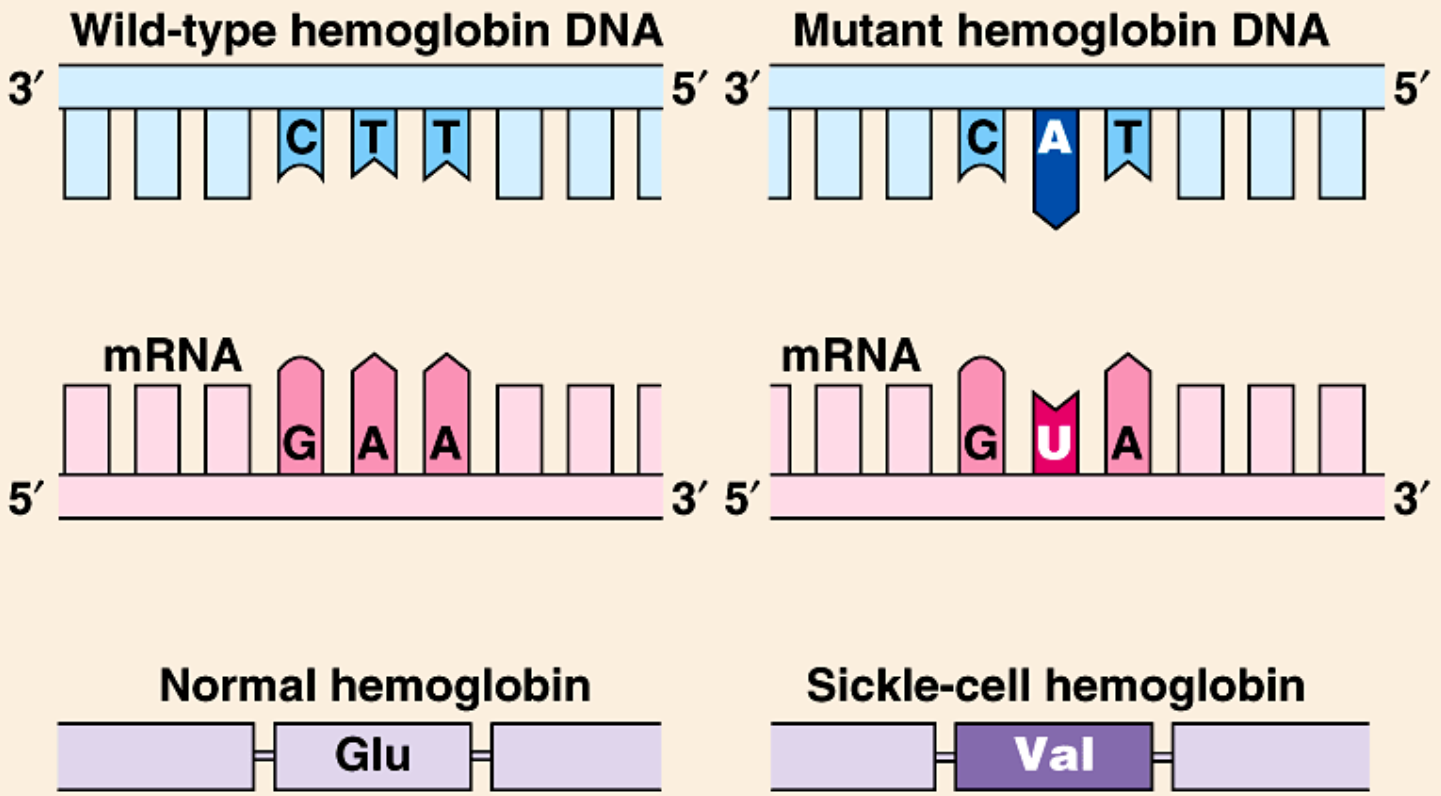
Point Mutations

- **Base-pair substitution**
  - The substitution of one nucleotide and its base-pairing partner with another pair of nucleotides
    - **Silent mutation**
      - no amino acid change
        - due to redundancy in code
    - **Missense mutation**
      - change amino acid
    - **Nonsense mutation**
      - change codon to stop codon
        - translation terminated prematurely

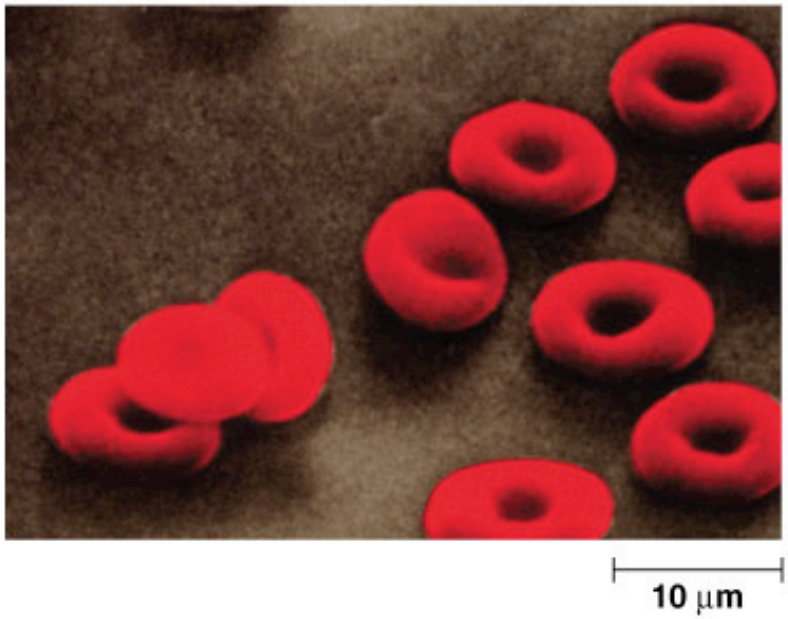


Point mutation leads to Sickle cell anemia

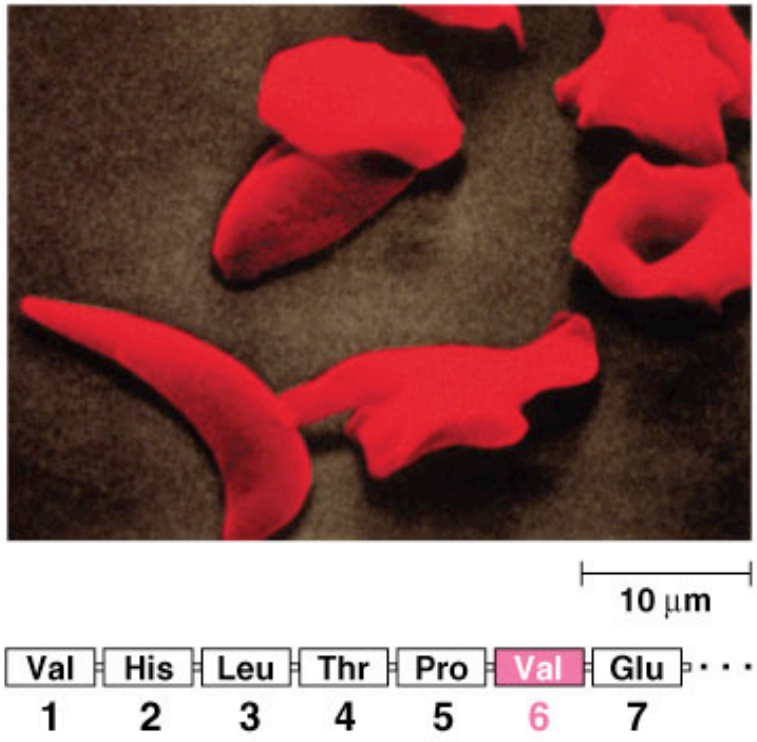
What kind of mutation?



Sickle cell anemia



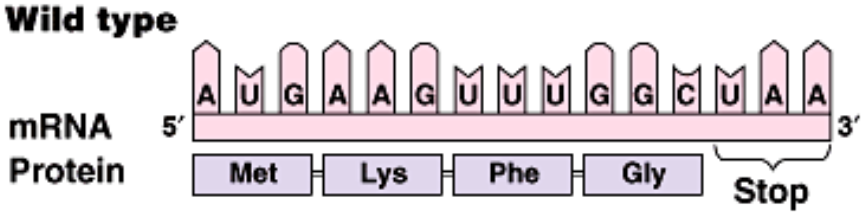
(a) Normal red blood cells and the primary structure of normal hemoglobin

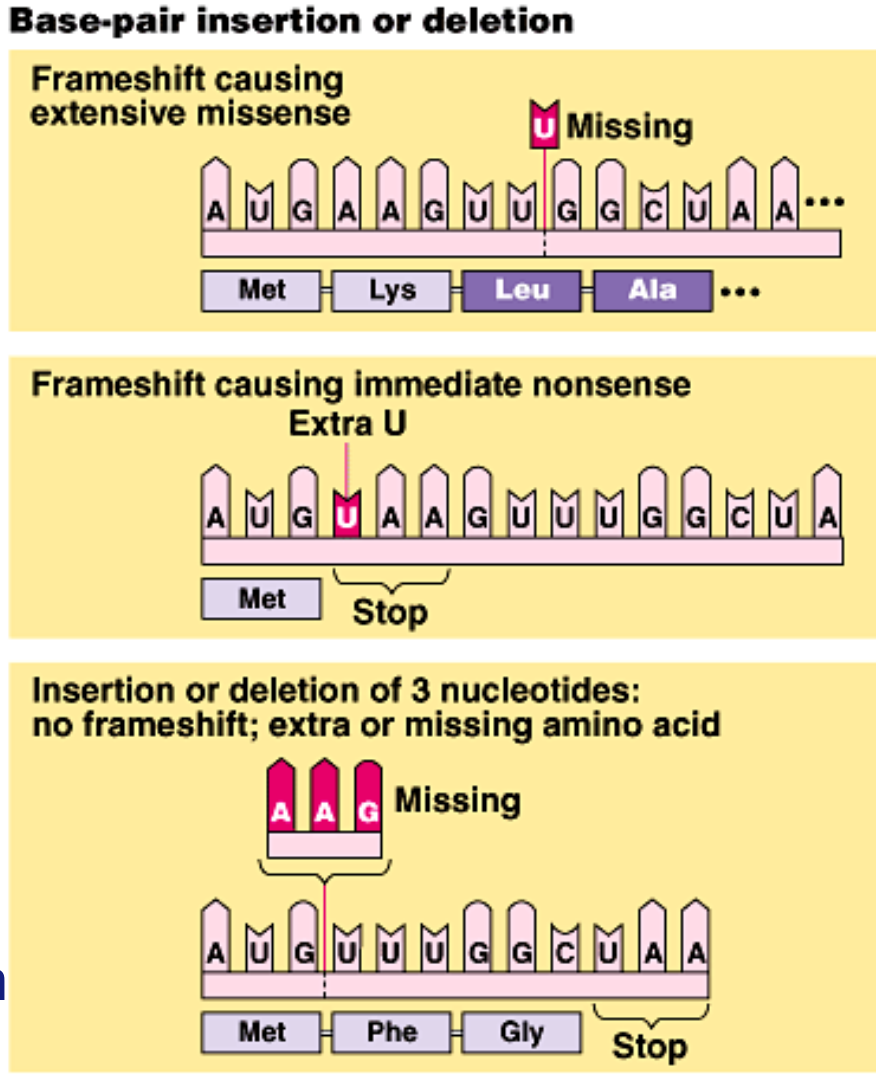


(b) Sickled red blood cells and the primary structure of sickle-cell hemoglobin

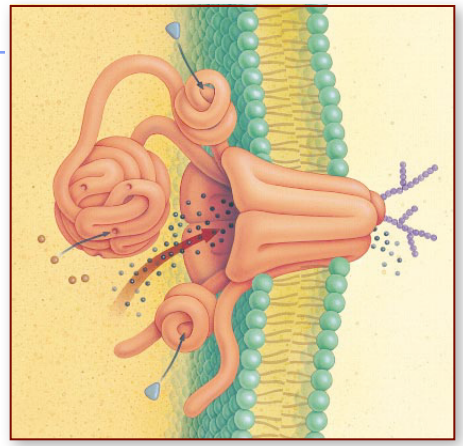
Point Mutations

- Insertions or deletions
  - Additions or losses of nucleotide pairs in a DNA gene
    - insertions
      - adding base(s)
    - deletions
      - losing base(s)
  - Frameshift Mutations
    - Cause a shift in the reading frame
      - Occurs when insertion or deletion is not a multiple of 3
    - changes everything "downstream" of mutation





Cystic fibrosis



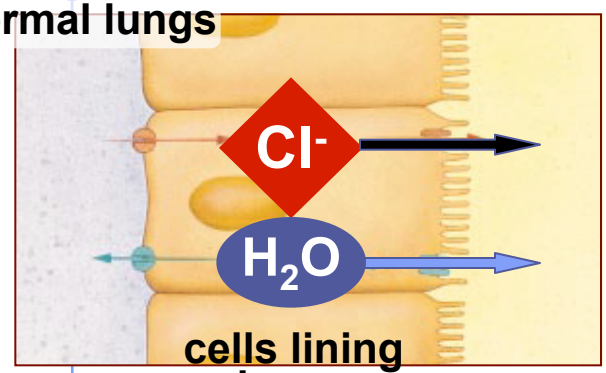
- Normal allele codes for a membrane protein that transports Cl^- across cell membrane
  - defective or absent channels limit transport of Cl^- (& H_2O) across cell membrane to the cell exterior
  - thicker & stickier mucus coats outside of cells
  - mucus build-up in the pancreas, lungs, digestive tract & causes bacterial infections

Effect on Lungs

Chloride channel: transports chloride through protein channel out of cell

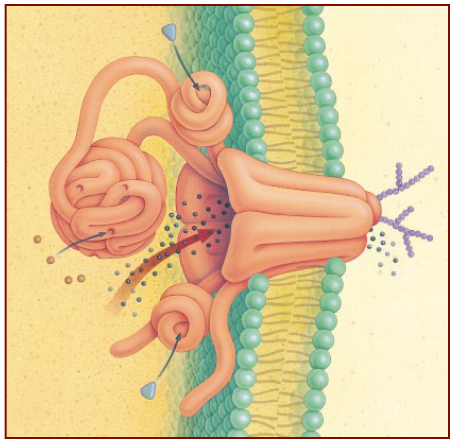
Osmotic effects: H_2O follows Cl^- & dilutes mucus to proper consistency

normal lungs

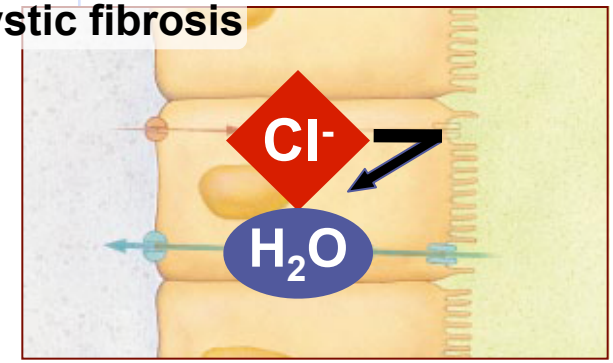


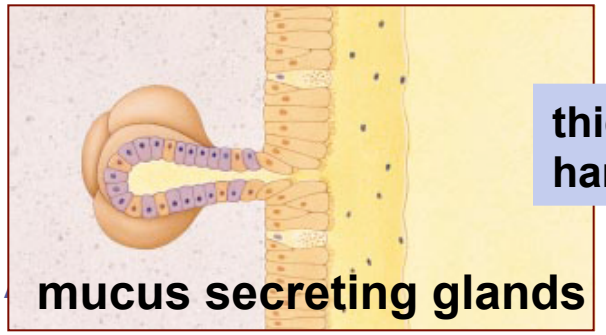
airway

Cl^- channel

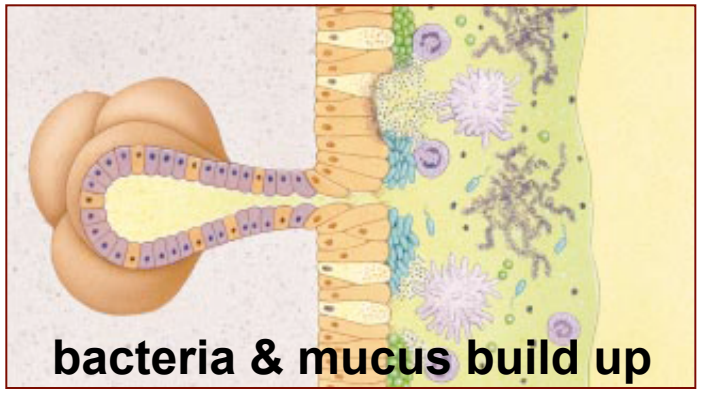


cystic fibrosis

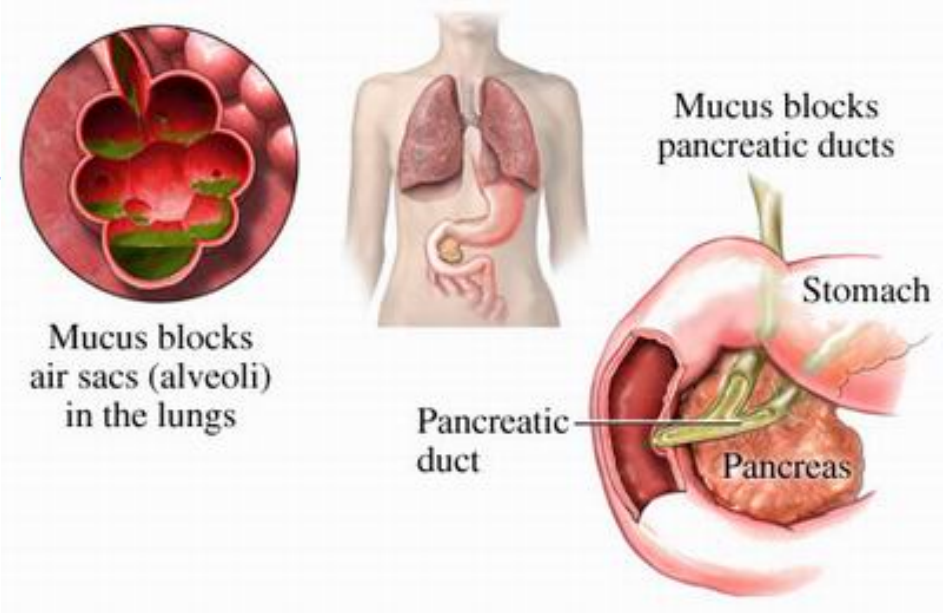


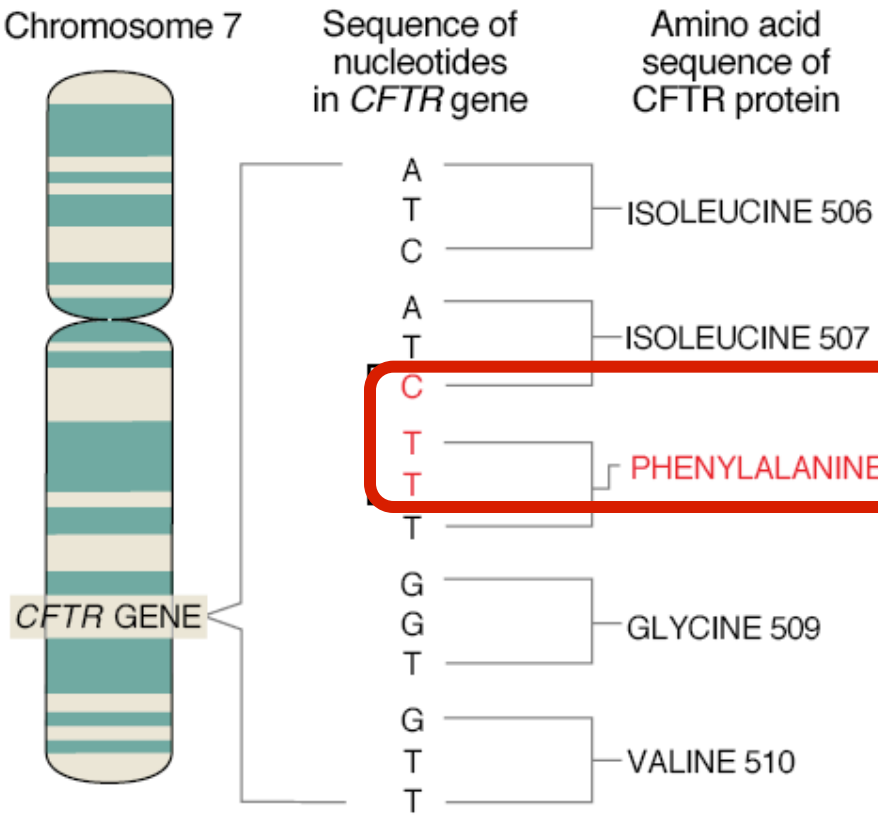


thickened mucus hard to secrete



Deletion leads to Cystic fibrosis

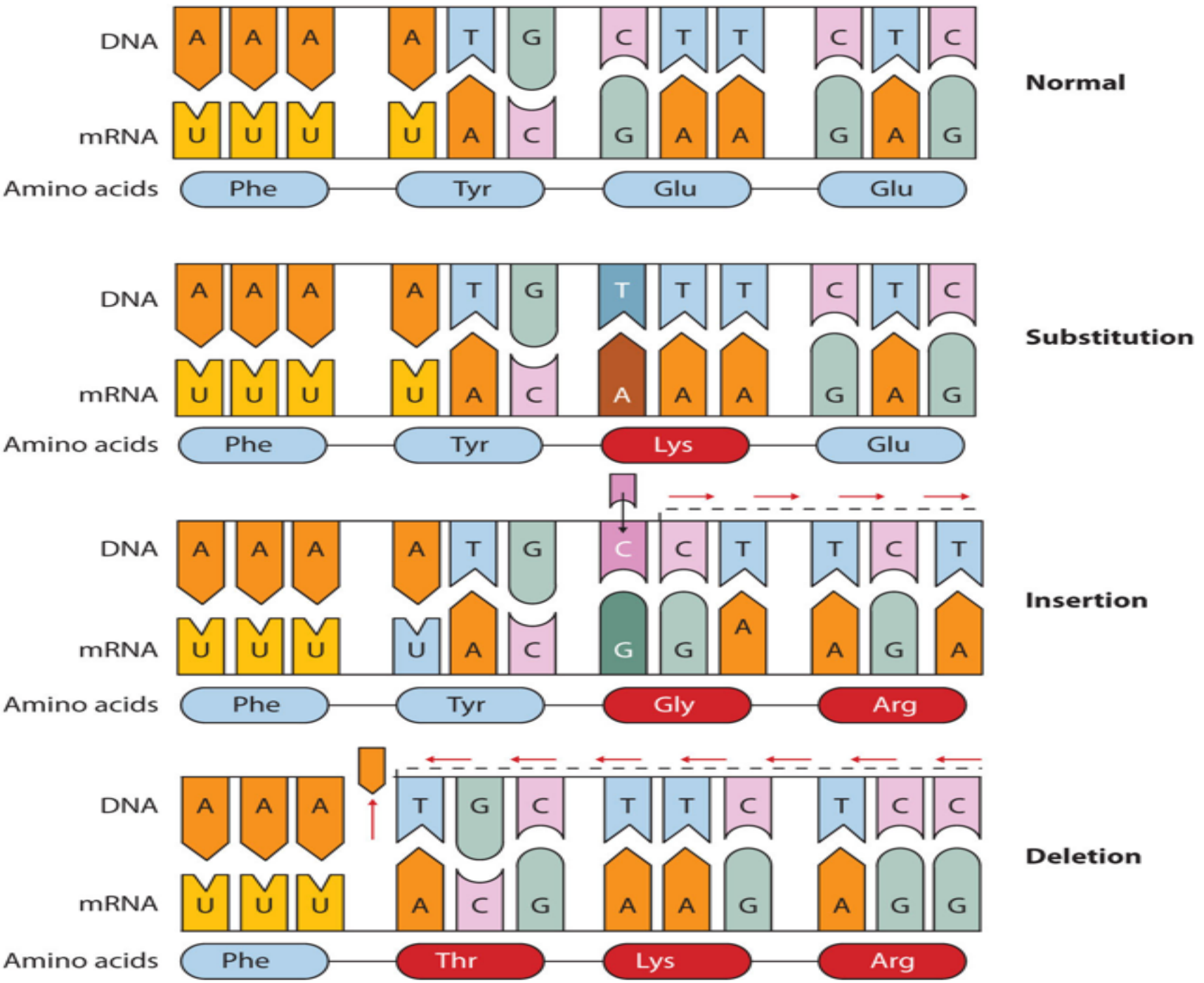




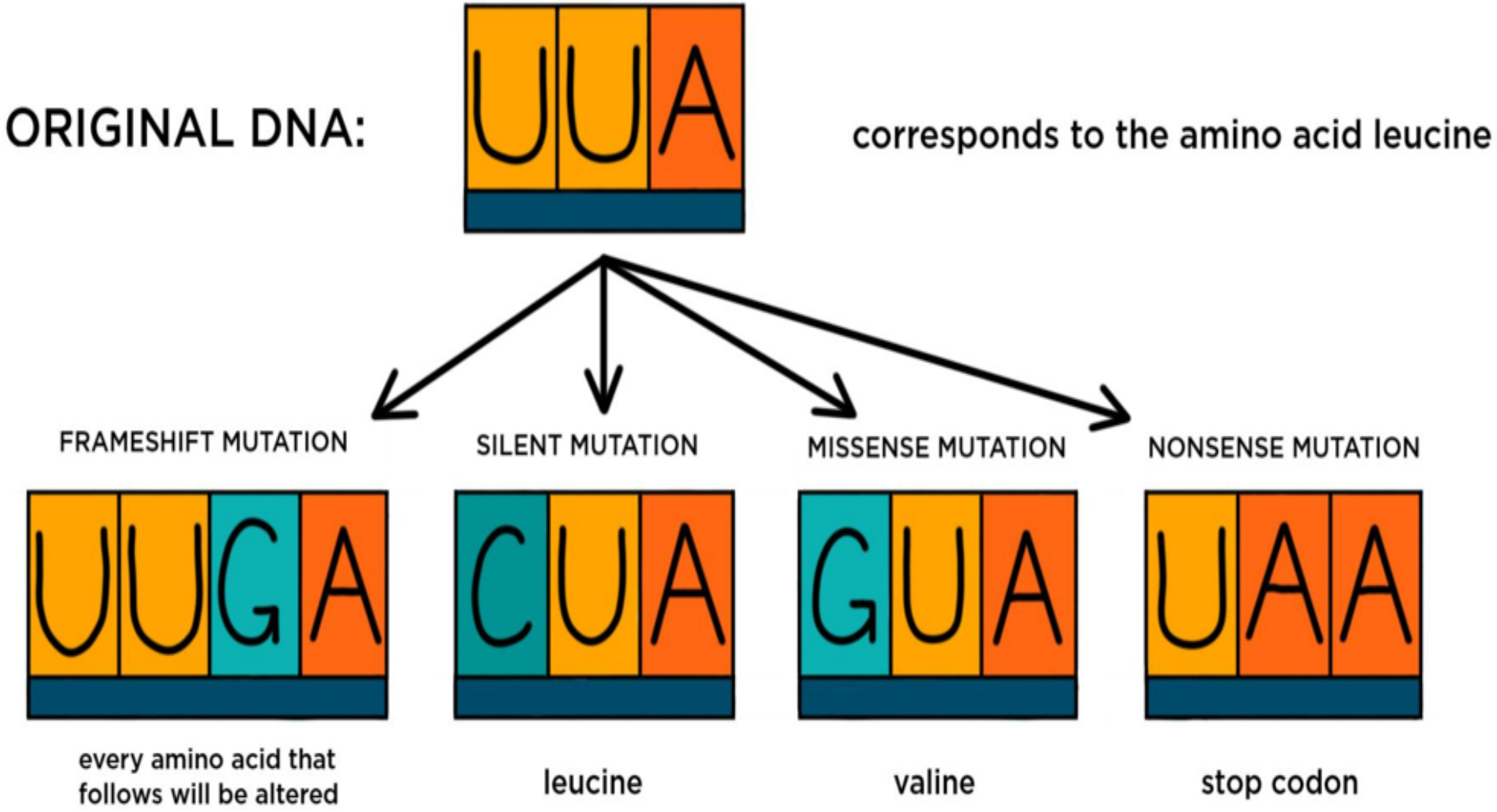
delta F508

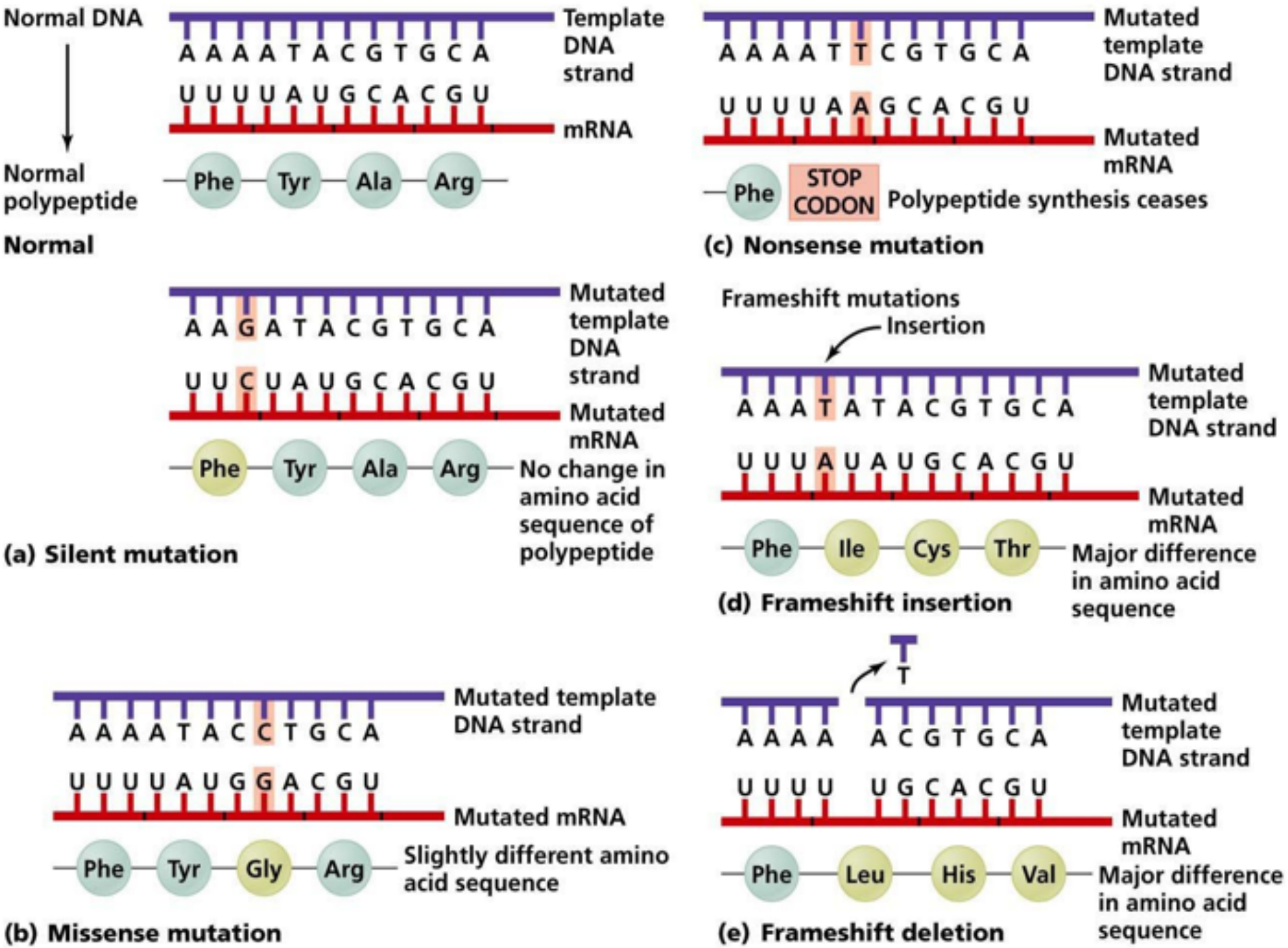
DELETED IN MANY PATIENTS WITH CYSTIC FIBROSIS

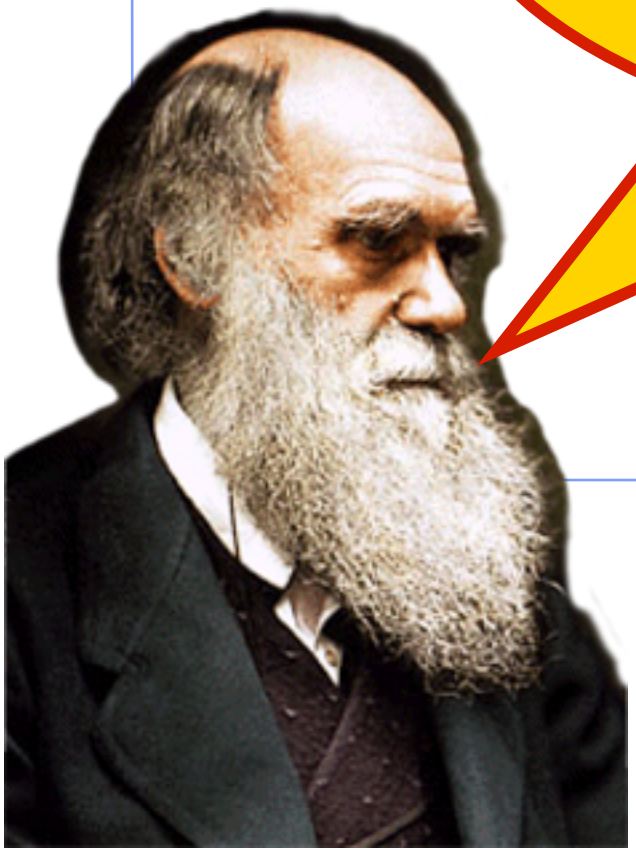
loss of one amino acid in polypeptide


DNA
A A A A T G C T T C T C
mRNA
U U U U A C G A A G A G
Amino acids
Phe Tyr Glu Glu
Normal
DNA
A A A A T G T T T C T C
mRNA
U U U U A C A A A G A G
Amino acids
Phe Tyr Lys Glu
Substitution
DNA
A A A A T G C C T T C T
mRNA
U U U U A C G G A A G A
Amino acids
Phe Tyr Gly Arg
Insertion
DNA
A A A T G C T T C T C C
mRNA
U U U A C G A A G A G G
Amino acids
Phe Thr Lys Arg
Deletion

What Are Point Mutations?




Normal DNA
A A A A T A C G T G C A
Template DNA strand
U U U U A U G C A C G U
mRNA
Normal polypeptide
Phe
Tyr
Ala
Arg
Normal
A A G A T A C G T G C A
Mutated template DNA strand
U U C U A U G C A C G U
Mutated mRNA
Phe
Tyr
Ala
Arg
No change in amino acid sequence of polypeptide
(a) Silent mutation
A A A A T A C C T G C A
Mutated template DNA strand
U U U U A U G G A C G U
Mutated mRNA
Phe
Tyr
Gly
Arg
Slightly different amino acid sequence
(b) Missense mutation
A A A A T T C G T G C A
Mutated template DNA strand
U U U U A A G C A C G U
Mutated mRNA
Phe
STOP CODON
Polypeptide synthesis ceases
(c) Nonsense mutation
Frameshift mutations
Insertion
A A A T A T A C G T G C A
Mutated template DNA strand
U U U A U A U G C A C G U
Mutated mRNA
Phe
Ile
Cys
Thr
Major difference in amino acid sequence
(d) Frameshift insertion
T
A A A A
A C G T G C A
Mutated template DNA strand
U U U U
U G C A C G U
Mutated mRNA
Phe
Leu
His
Val
Major difference in amino acid sequence
(e) Frameshift deletion



What's the value of mutations?