Enrichment Course in Biology

Molecular Biology

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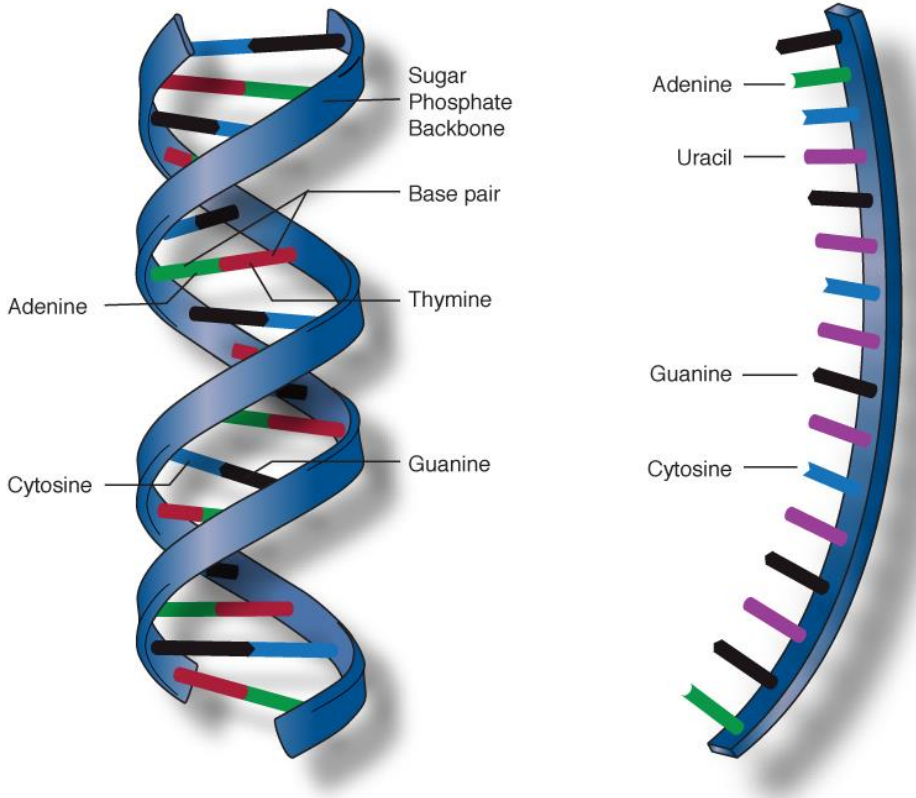
Learning Outcomes

- Describe the process of gene expression and protein synthesis
- List and define the different types of mutation

Nucleic acid



Deoxyribonucleic acid (DNA)

Ribonucleic acid (RNA)

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Illustration by Darryl Leja, NHGRI

Nucleic acids

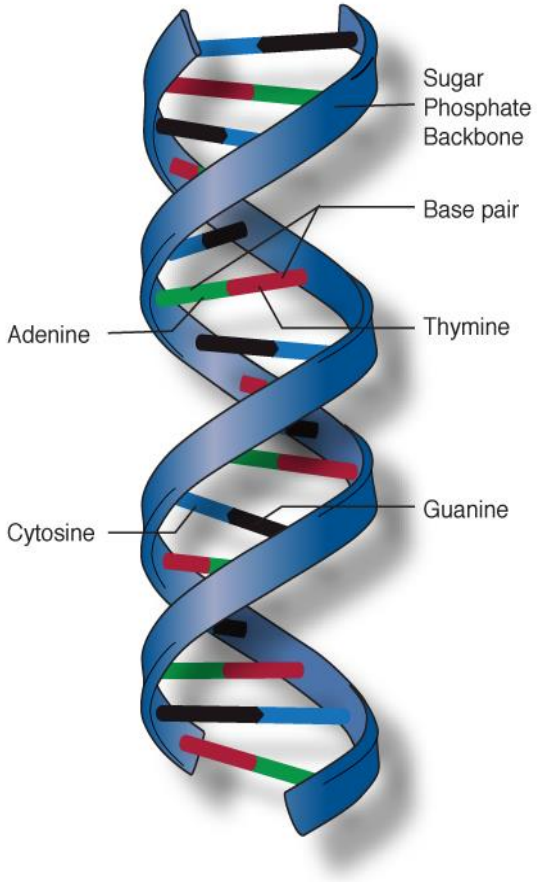
- Nucleic acid is a polymer
  - Formed by linking nucleotides

through phosphodiester bonds

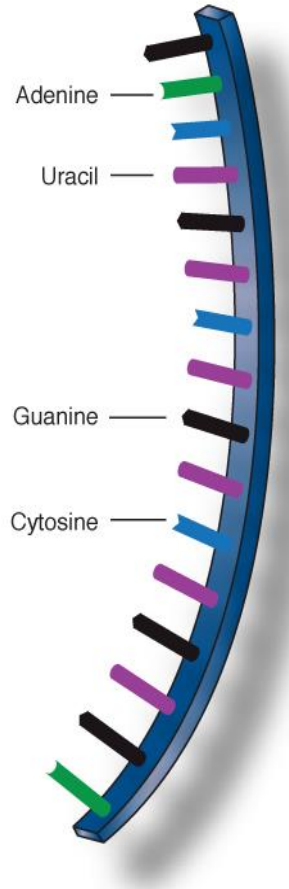
Nucleotides

1. A nitrogen containing base
2. A pentose (sugar)
3. 1-3 phosphate groups

There are five different bases
A = adenine
G = guanine
C = cytosine
T = thymine
U = uracil



Deoxyribonucleic acid
(DNA)



Ribonucleic acid
(RNA)

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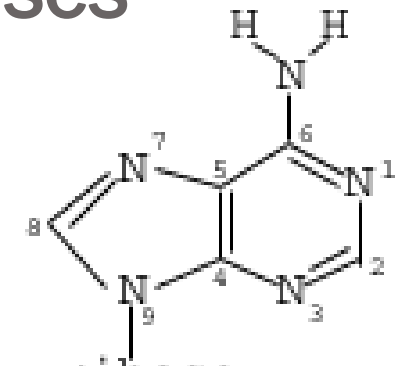
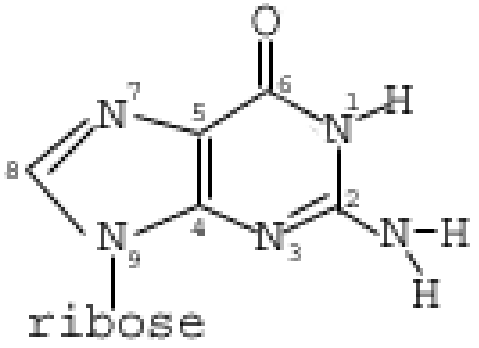
Structure of bases

- For your reference only!

Purines

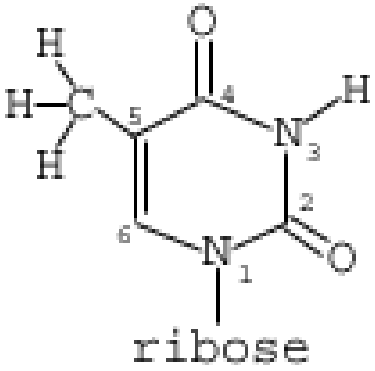


adenosine

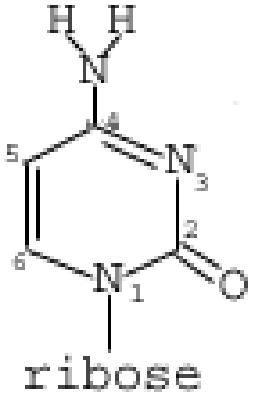


guanine

Pyrimidines



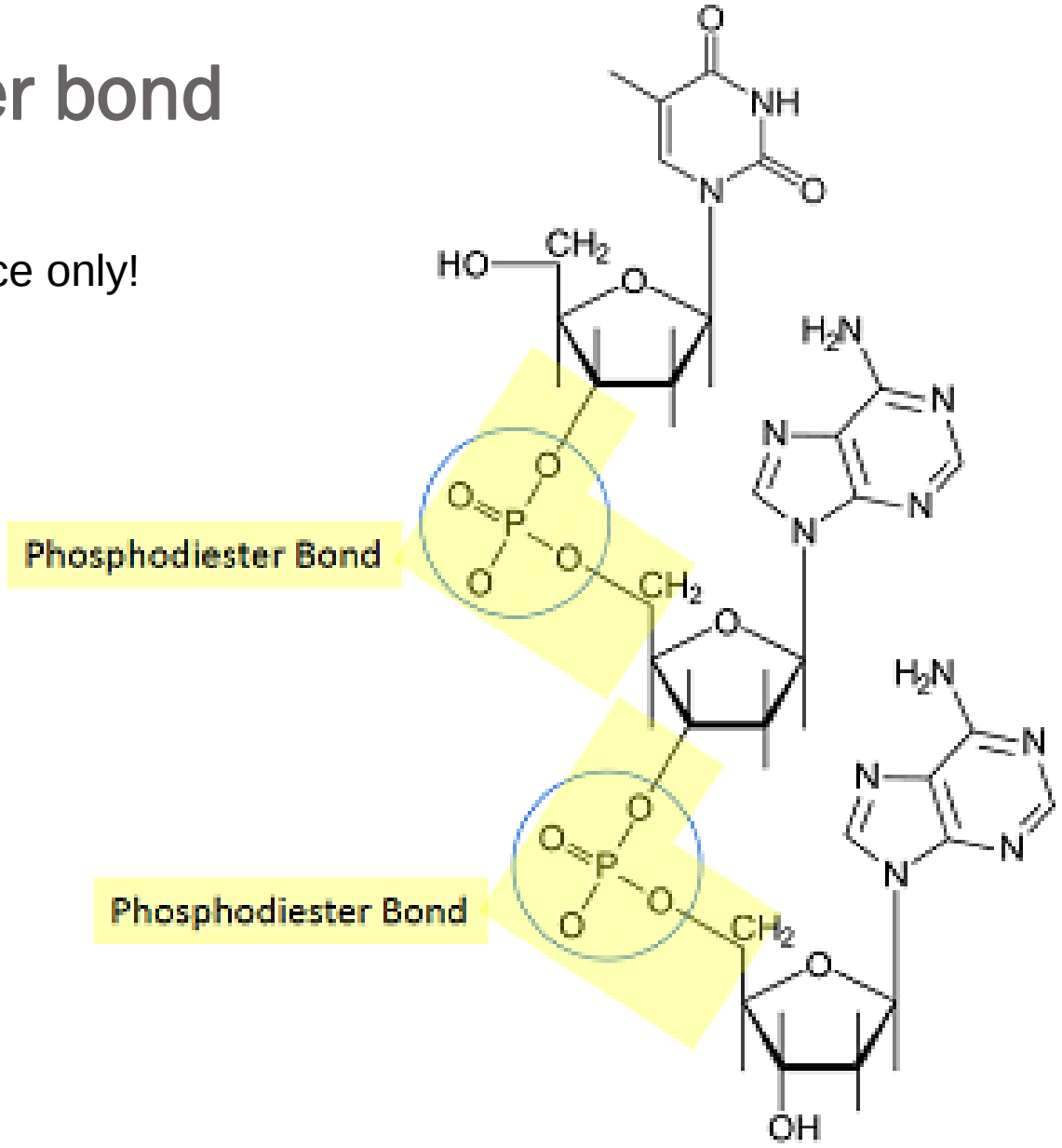
thymine



cytosine

Phosphodiester bond

- For your reference only!



Characteristics of DNA

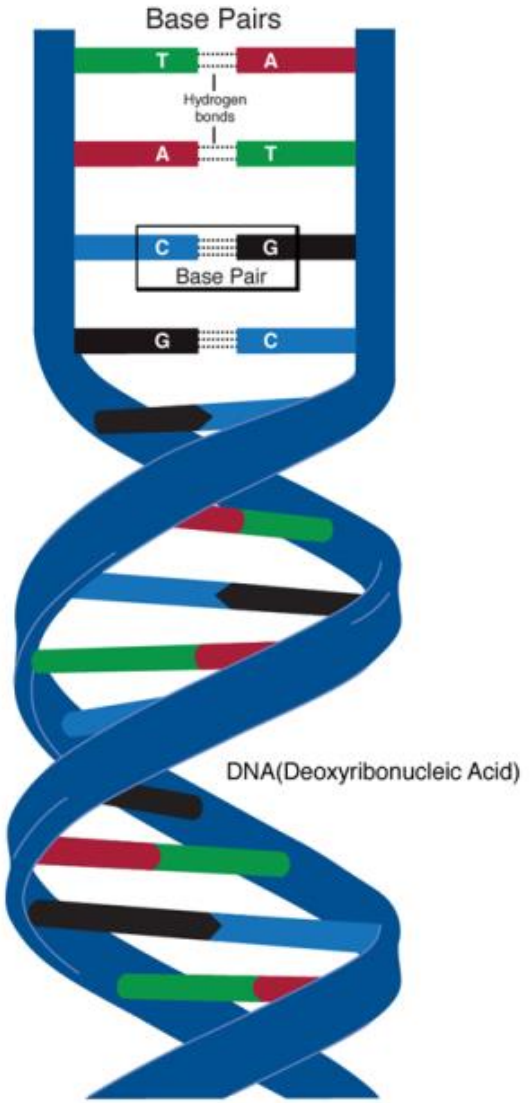
- DNA is double-stranded aligned in anti-parallel fashion
- Two strands held together by hydrogen bonds formed between the bases
- Complementary base pairing
  - A must pair up with T (2 hydrogen bonds)
  - G must par up with C (3 hydrogen bonds)
- Forms helical structure
- Sugar phosphate backbone on surface

  Base-pair in the center

  $\rightarrow$ accounts for stability of DNA
- Major grooves and minor grooves
  - For protein binding
- Wraps around histone proteins
  - For condensation

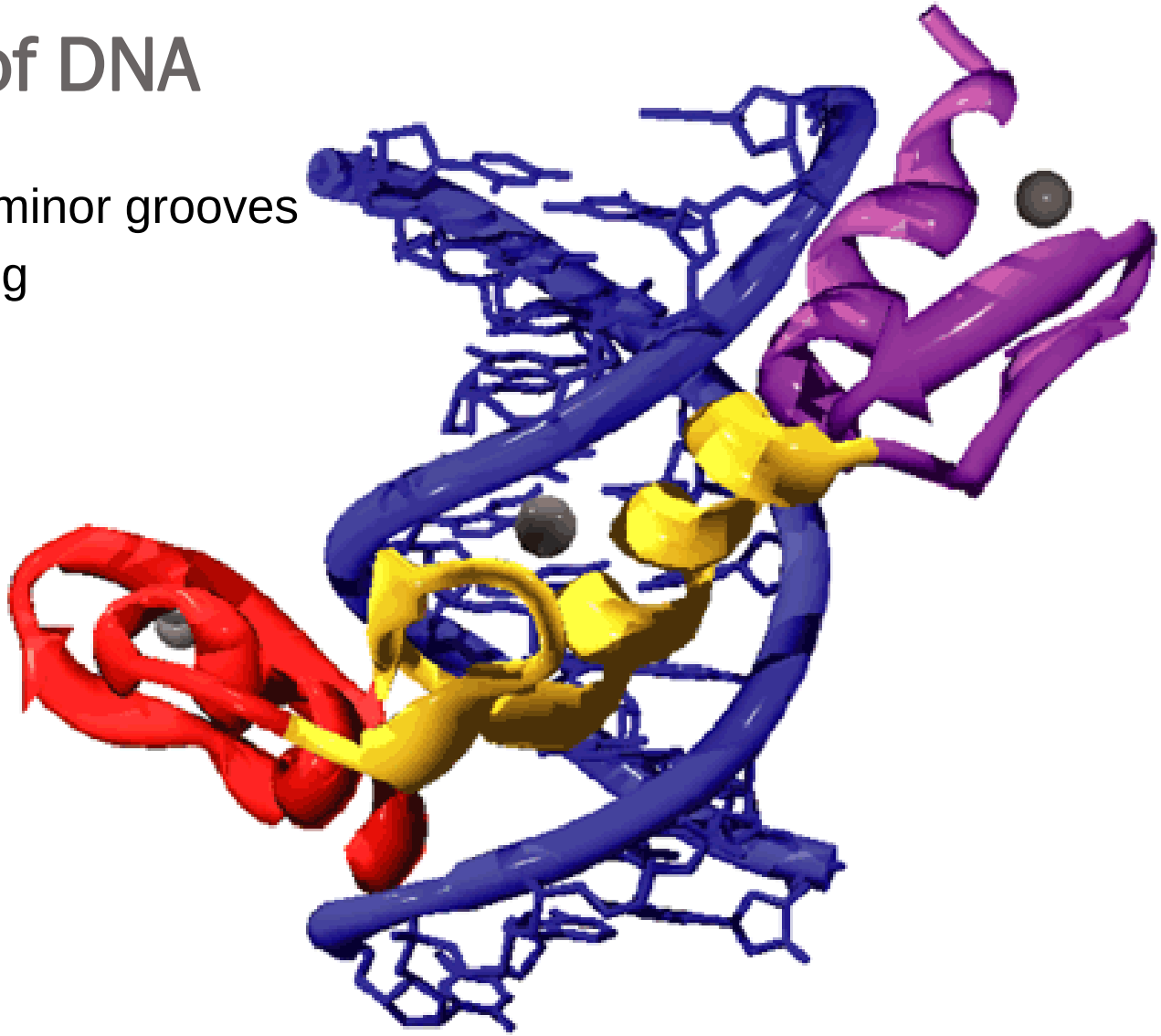
Characteristics of DNA

- Complementary base pairing
  - A must pair up with T (2 hydrogen bonds)
  - G must par up with C (3 hydrogen bonds)



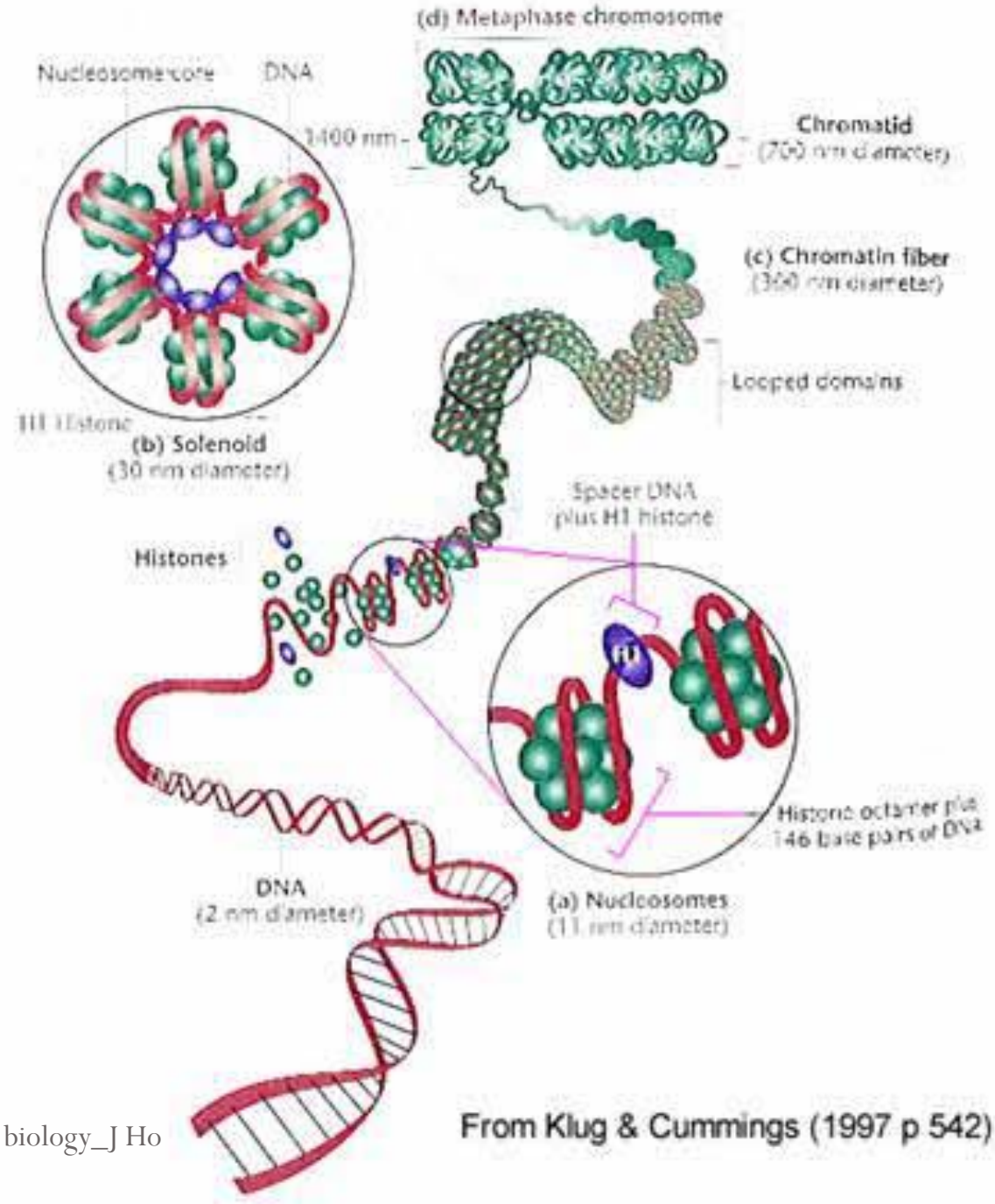
Characteristics of DNA

- Major grooves and minor grooves
  - For protein binding



http://www.nature.com/nrd/journal/v2/n5/fig_tab/nrd1087_F1.html

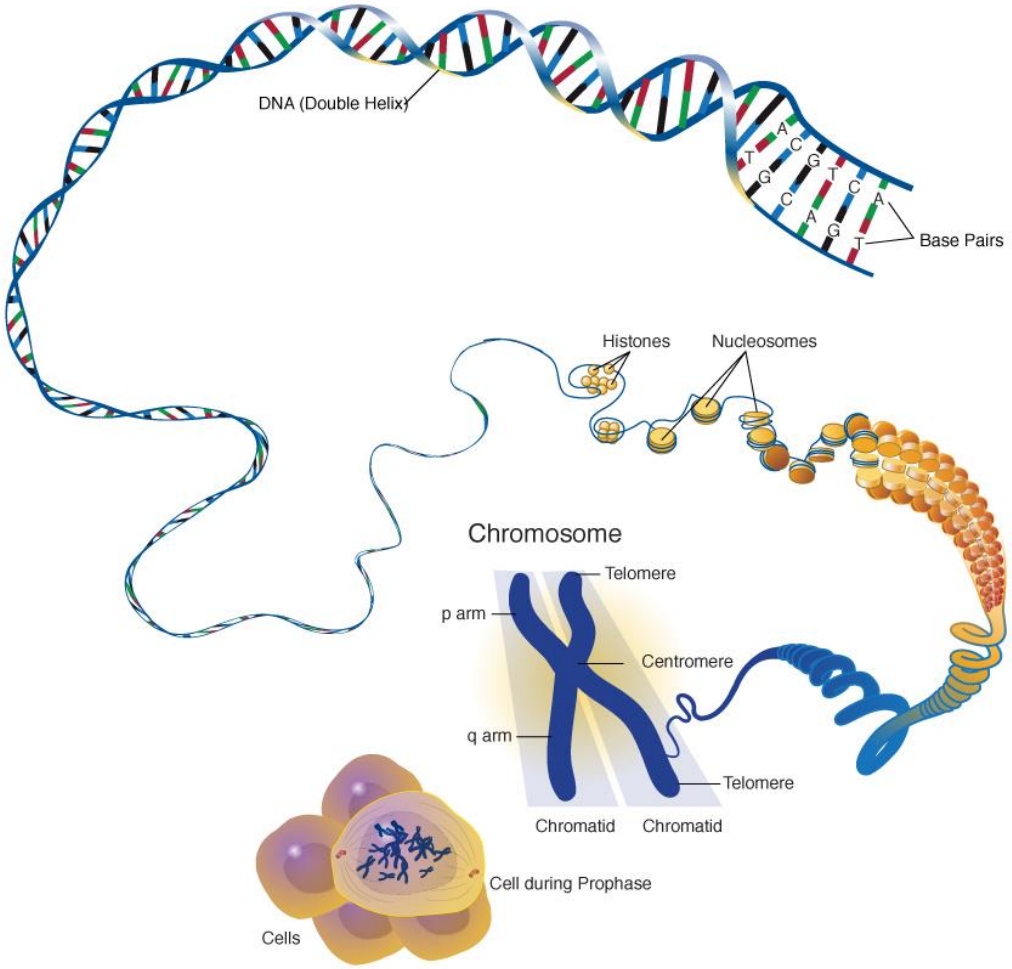
From DNA to chromosome



From Klug & Cummings (1997 p 542)

http://www.carolguze.com/text/102-7-eukaryoticcells.shtml

Chromosome



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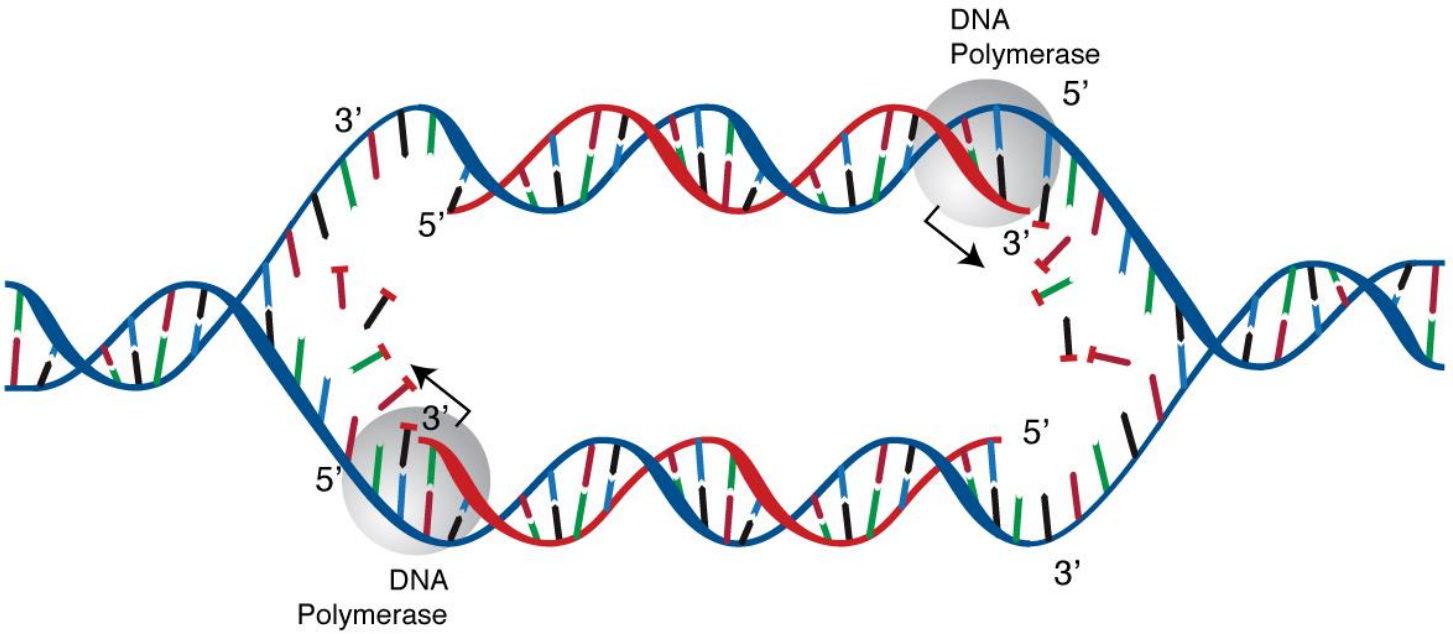

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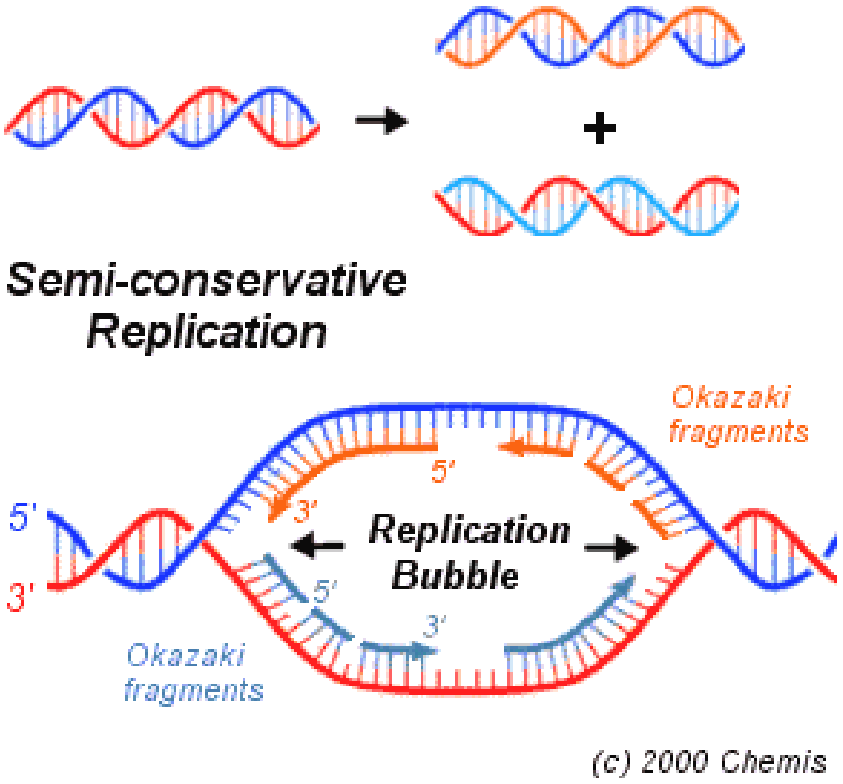
Replication: duplication of DNA

1. Occurs in nucleus during cell division
   a. Mitosis
   b. Meiosis
2. DNA unwinds
3. Each strand serves as a template
   - By complementary base pairing,

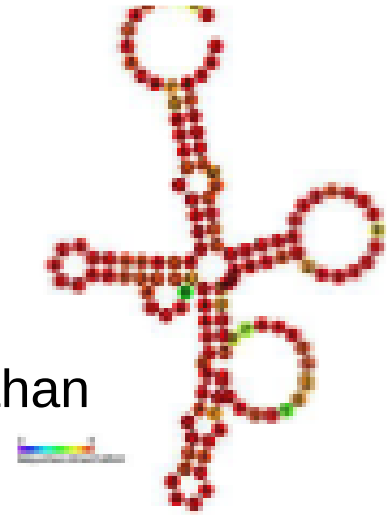
   Another new strand is added by DNA polymerase
4. Semi-conservative DNA replication

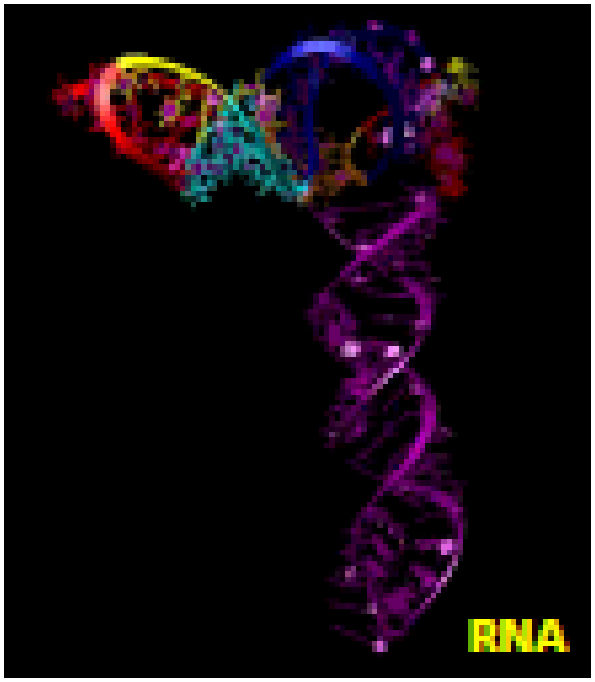


http://www.tokresource.org/tok_classes/biobiobio/biomenu/dna_replication/index.htm

Characteristics of RNA

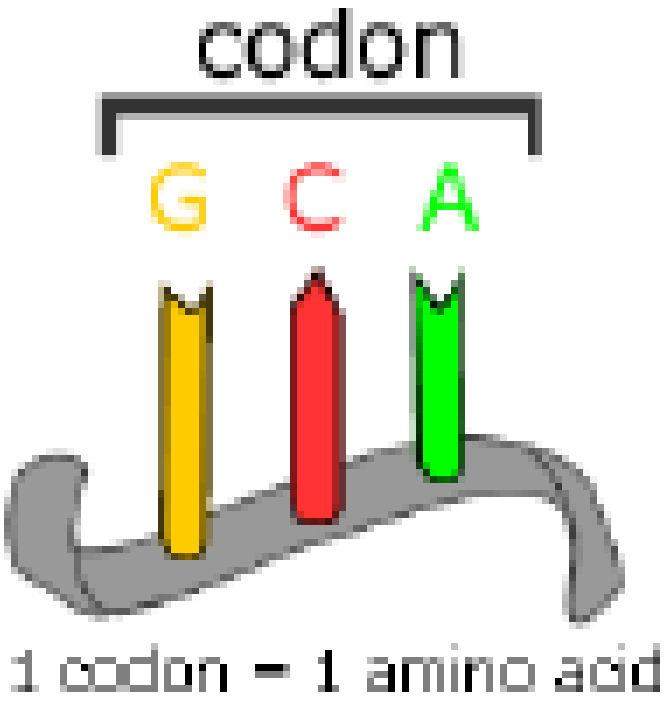
1. Contains uracil instead of thymine
2. 3 types of RNA
   a. Messenger RNA (mRNA)
   b. Ribosomal RNA (rRNA)
   c. Transfer RNA (tRNA)
3. Made from DNA through transcription
4. All involved in protein biosynthesis
5. Single-stranded (less stable than DNA)
6. Forms secondary structure
   a. Hairpin loops
   b. Has 3D sturcture





DNA is the code of life

- What does DNA used for coding?
  - A
  - T
  - G
  - C
- What does DNA code for and how?



Genetic Code

Stop codons:

UAA
UAG
UGA

RNA codon table

1st position	2nd position U	2nd position C	2nd position A	2nd position G	3rd position
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	stop	stop	A
	Leu	Ser	stop	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G
		Amino Acids			

Ala: Alanine
Arg: Arginine
Asn: Asparagine
Asp:Aspartic acid
Cys:Cysteine
Gln: Glutamine
Glu: Glutamic acid
Gly: Glycine
His: Histidine
Ile: Isoleucine
Leu: Leucine
Lys: Lysine
Met: Methionine
Phe: Phenylalanine
Pro: Proline
Ser: Serine
Thr: Threonine
Trp: Tryptophane
Tyr: Tyrosisne
Val: Valine

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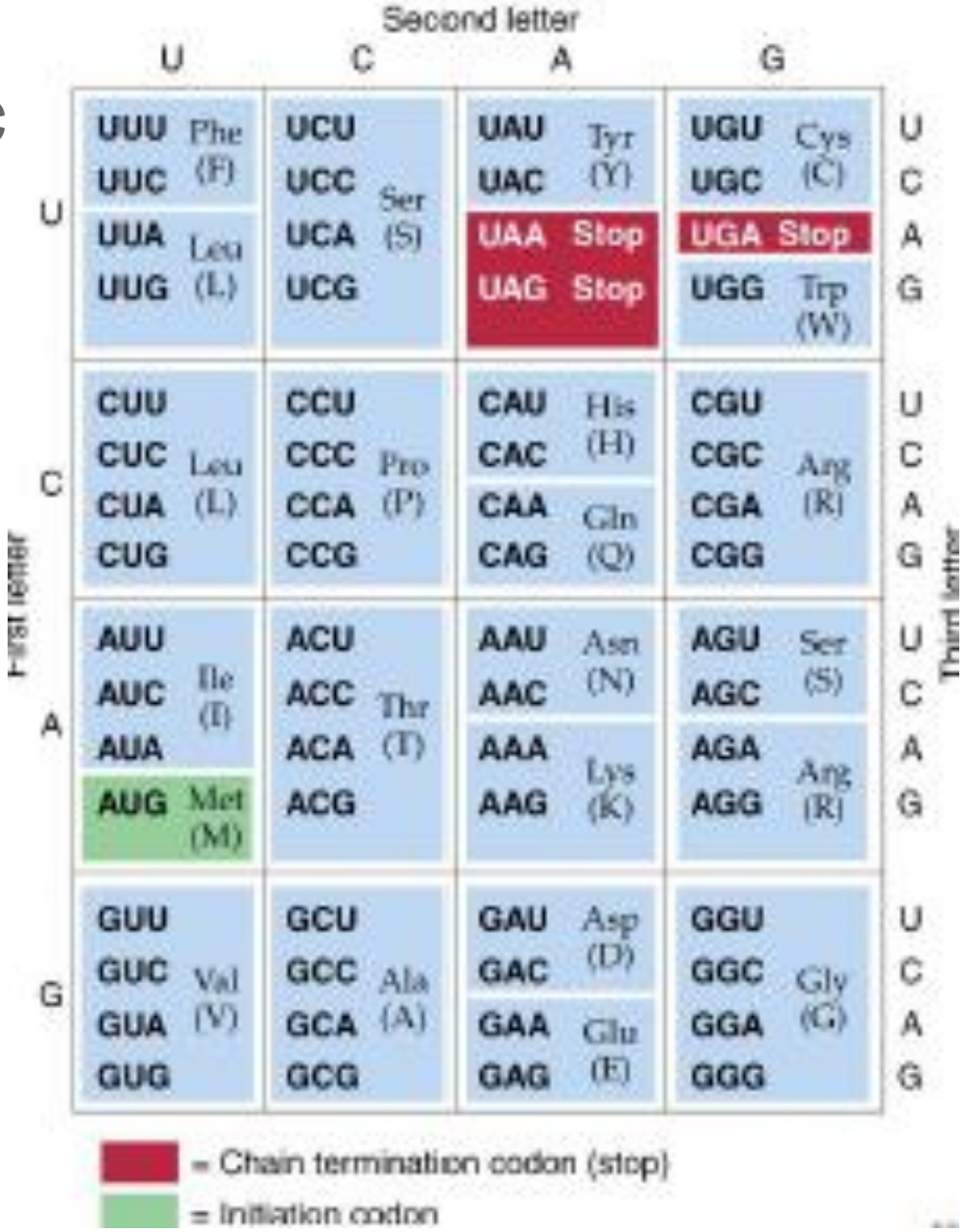
The universal genetic code

1. 64 codons
2. 20 amino acids
3. Most amino acids have more than one codon
   a. Codon degeneracy
   b. Synonym
4. A common start codon (AUG)

Serves as start signal for protein synthesis

5. 3 stop codons serve to signal the end of protein synthesis.



How does DNA transfer its information to make protein?

DNA

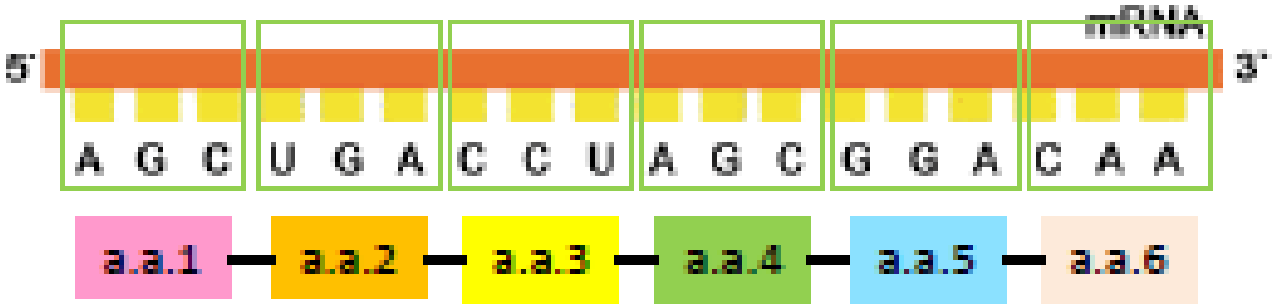
RNA

Protein

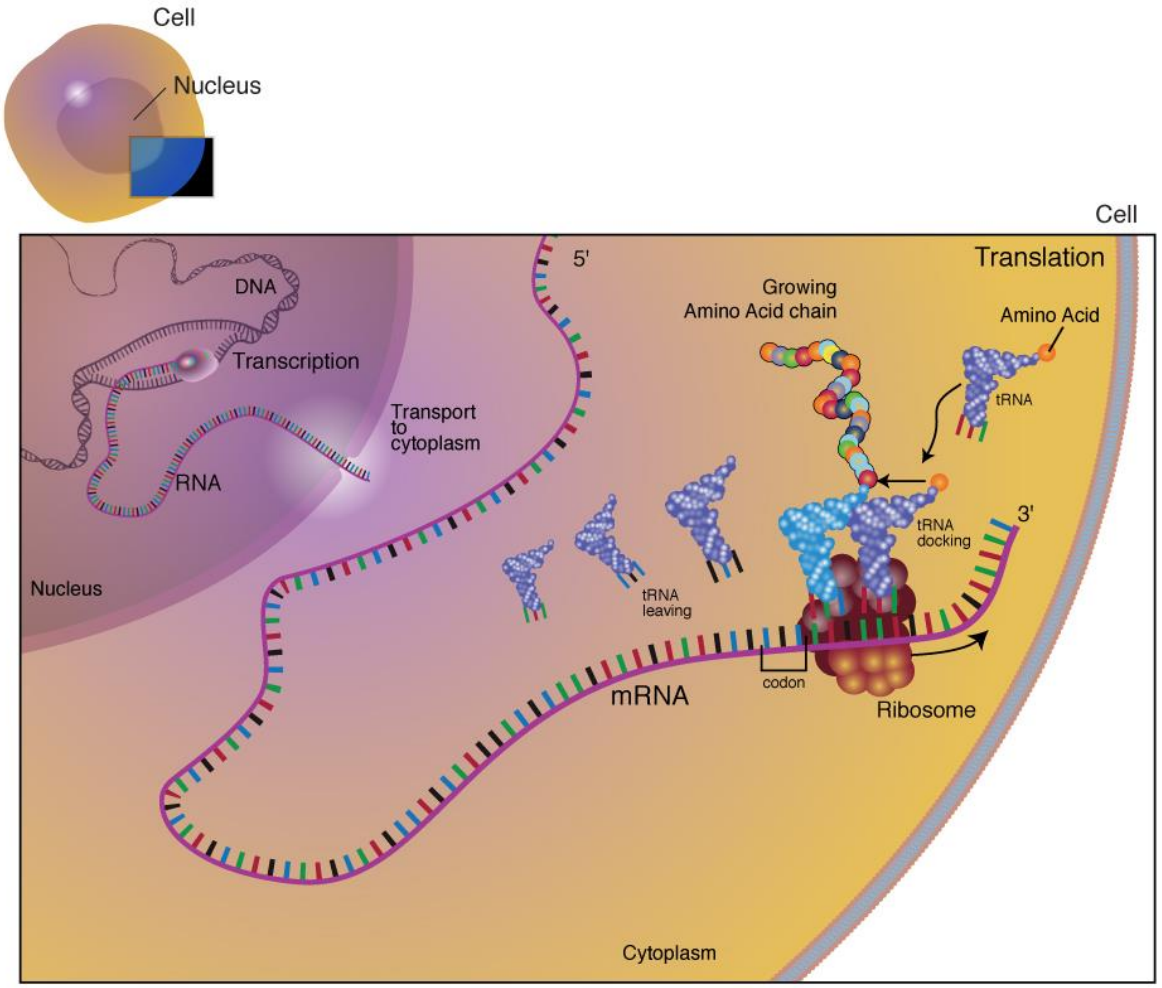
Transcription: transfer information (code) from DNA to RNA

DNA	RNA
A	A
T	U
G	G
C	C

Translation: code on RNA (from DNA) is read to make protein



Translation



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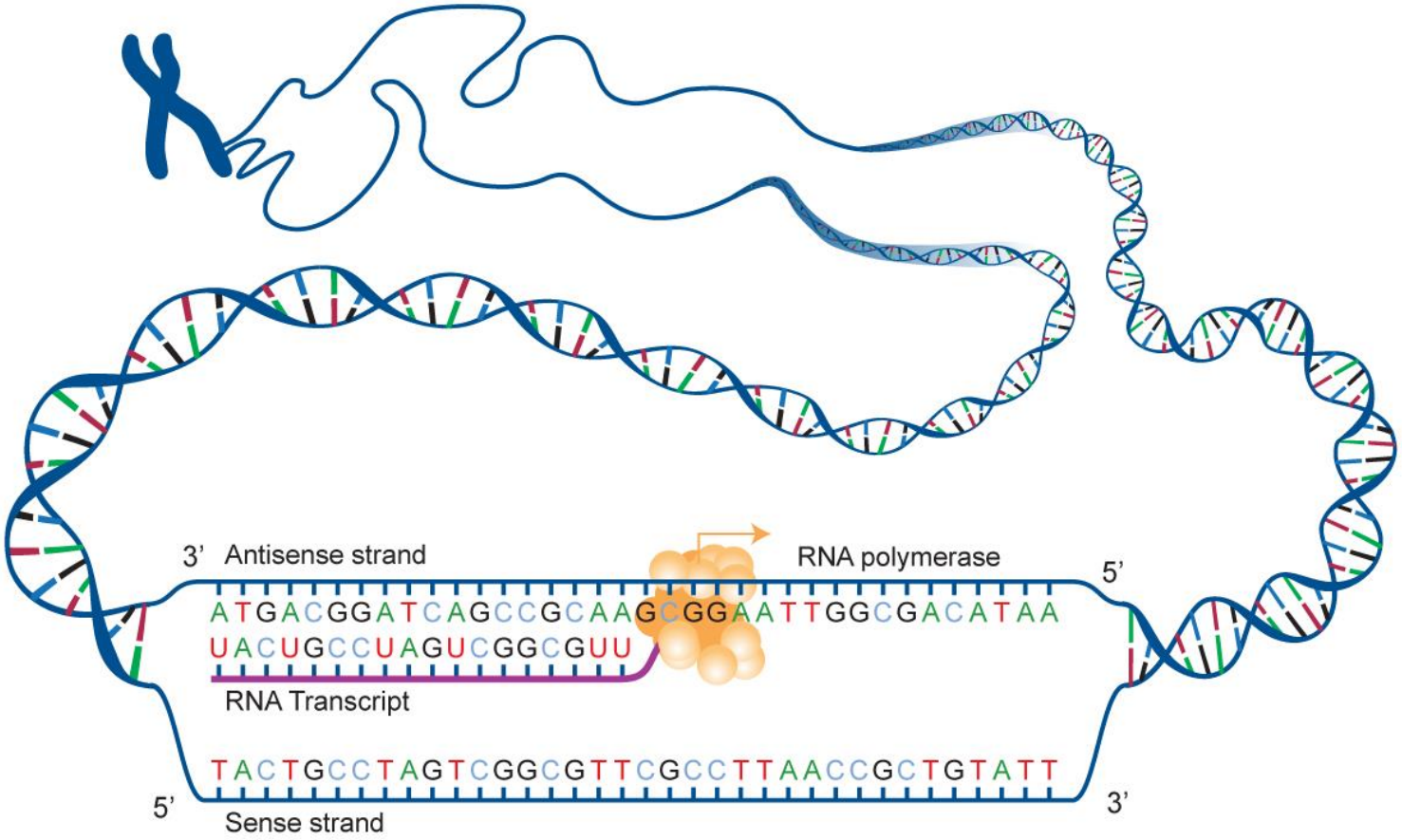
Transcription



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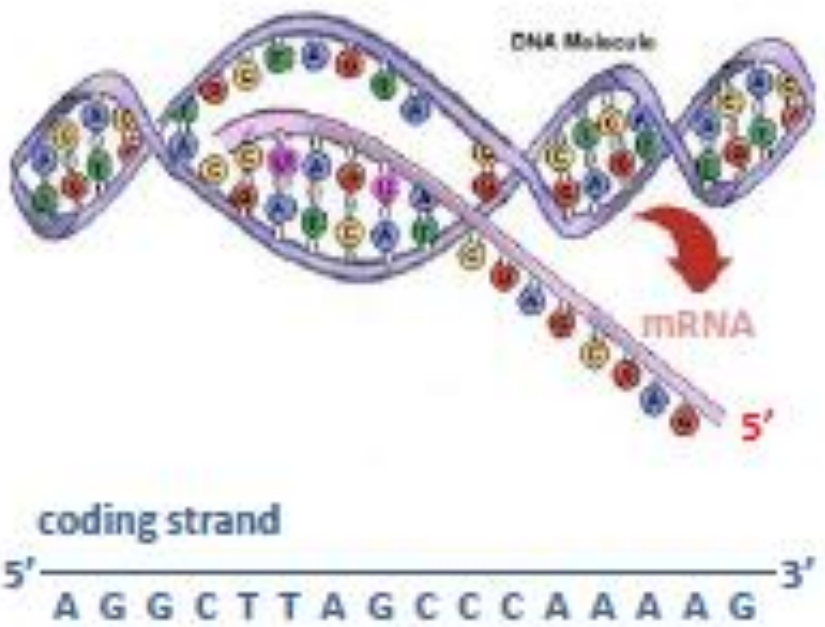
Transcription: transfer information (code) from DNA to mRNA

1. Occurs in nucleus
2. A controlled process

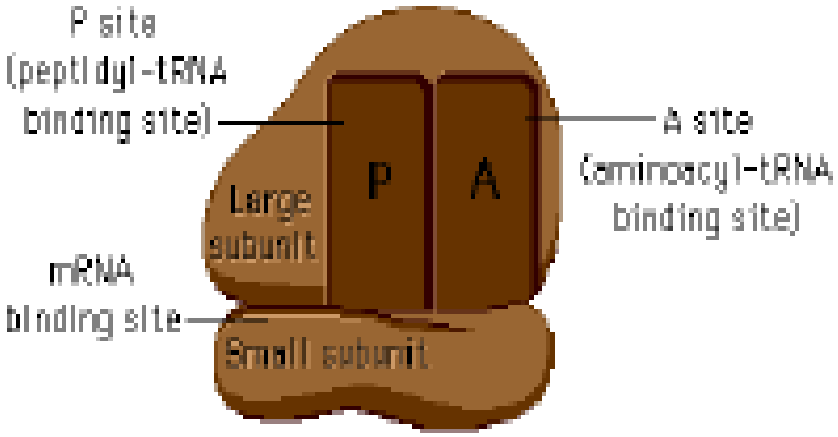
   e.g. controlled by hormones
3. DNA unwinds
4. One of the strand (coding strand) is used as template for RNA synthesis

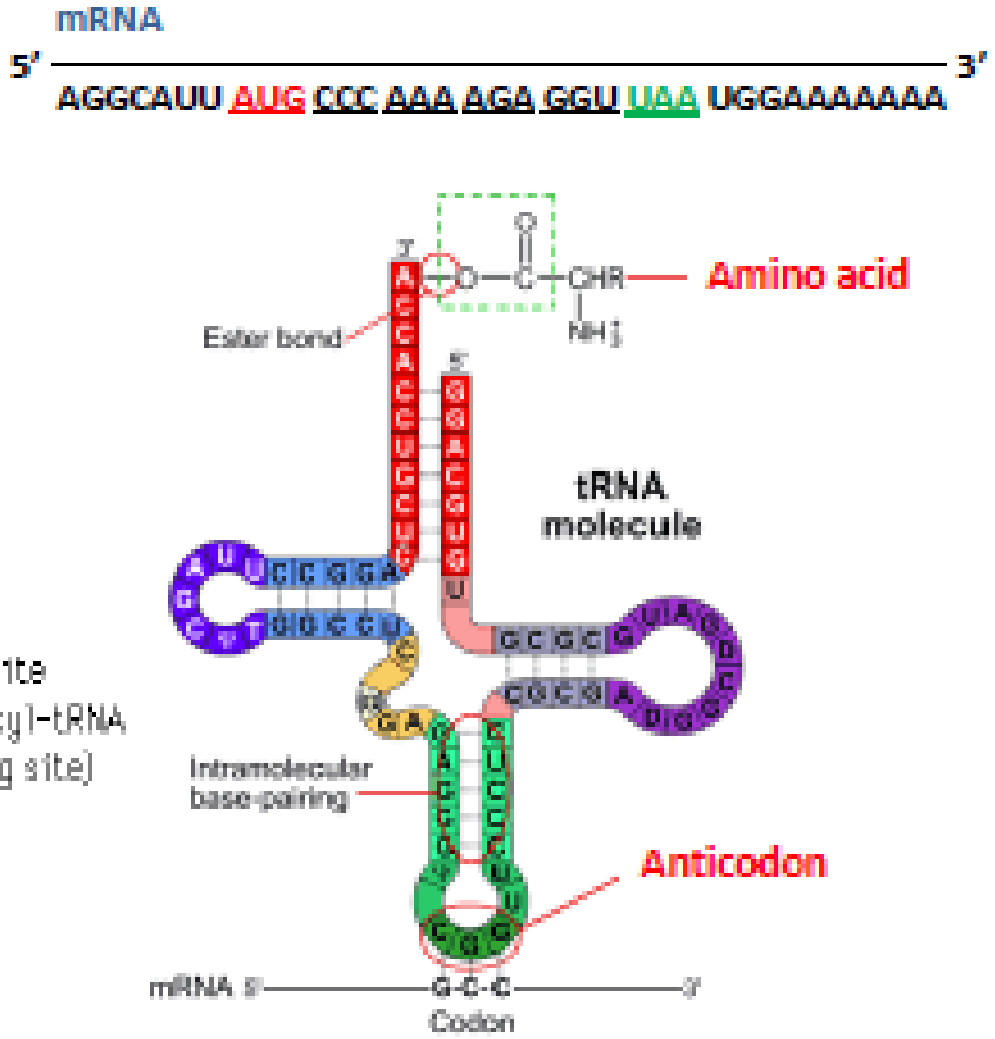
   - By complementary base pairing, RNA is made by RNA polymerase
5. DNA rewinds at the other side as transcription continues

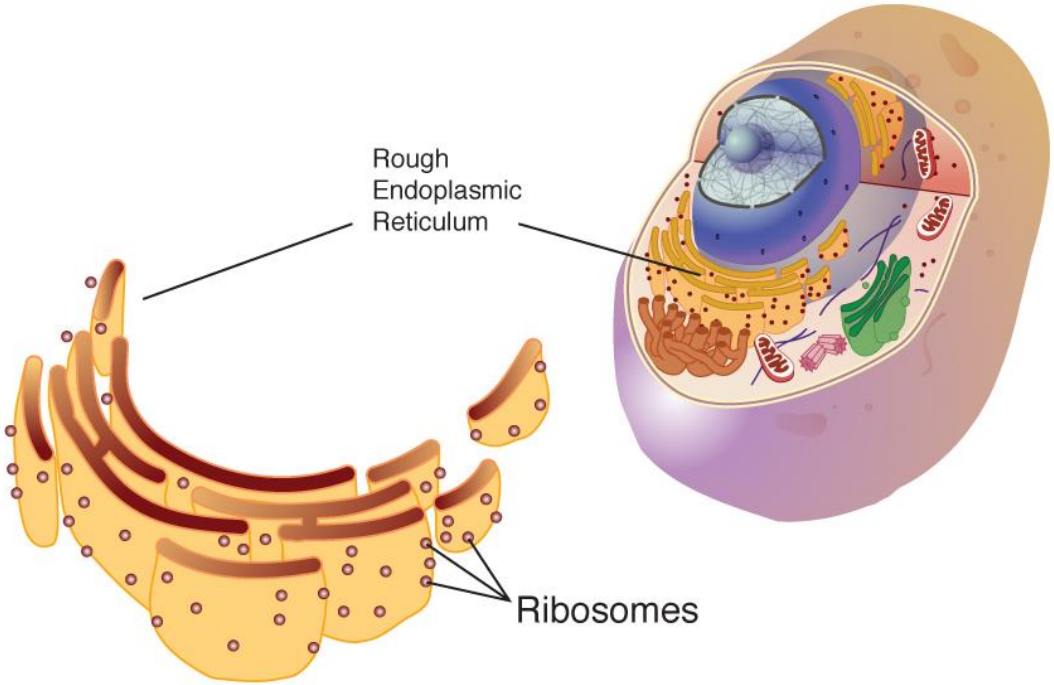


Translation: code on mRNA is read to make protein

1. Occurs in cytoplasm
2. Requires
   a. mRNA (template)
   b. tRNA (carry amino acids)
   c. rRNA (part of ribosome)
   d. Ribosome
      - Large subunit (P site, A site)
      - Small subunit







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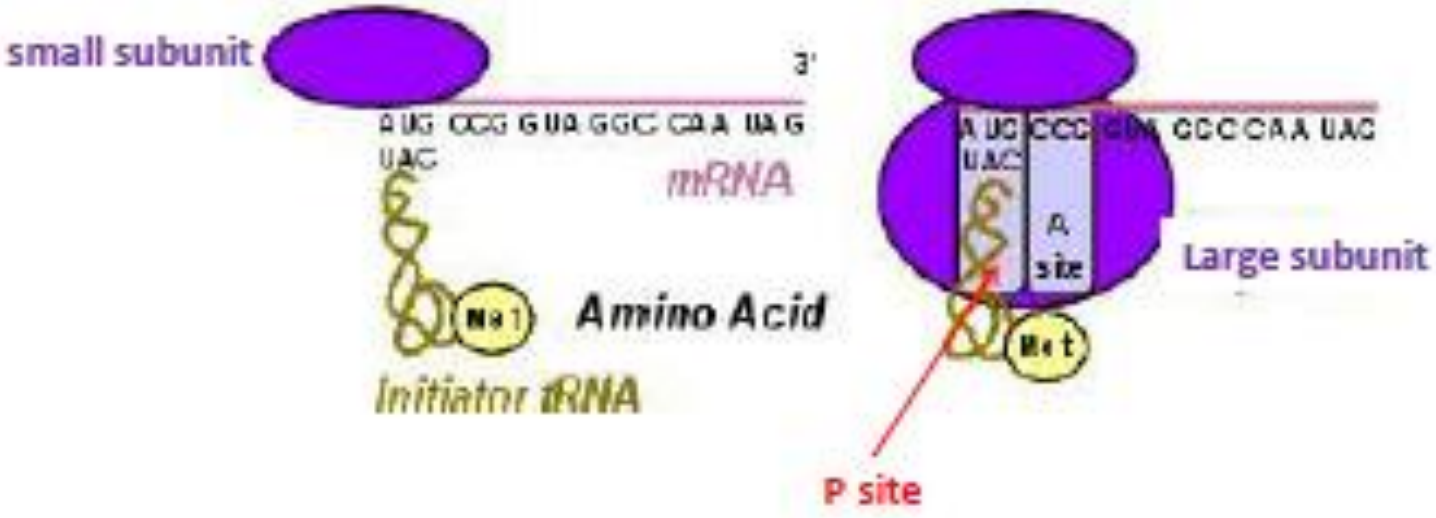
Translation: code on mRNA is read to make protein

- The 3 steps of translation: initiation, chain elongation and termination

1. Initiation: assembly of ribosome at the start site (AUG)
   a. Small subunit and the initiator tRNA (Met-rRNA^{Met}) bind first
   b. Then the large subunit binds
   c. Initiator rRNA occupies P site



Translation: code on mRNA is read to make protein

2. Chain elongation

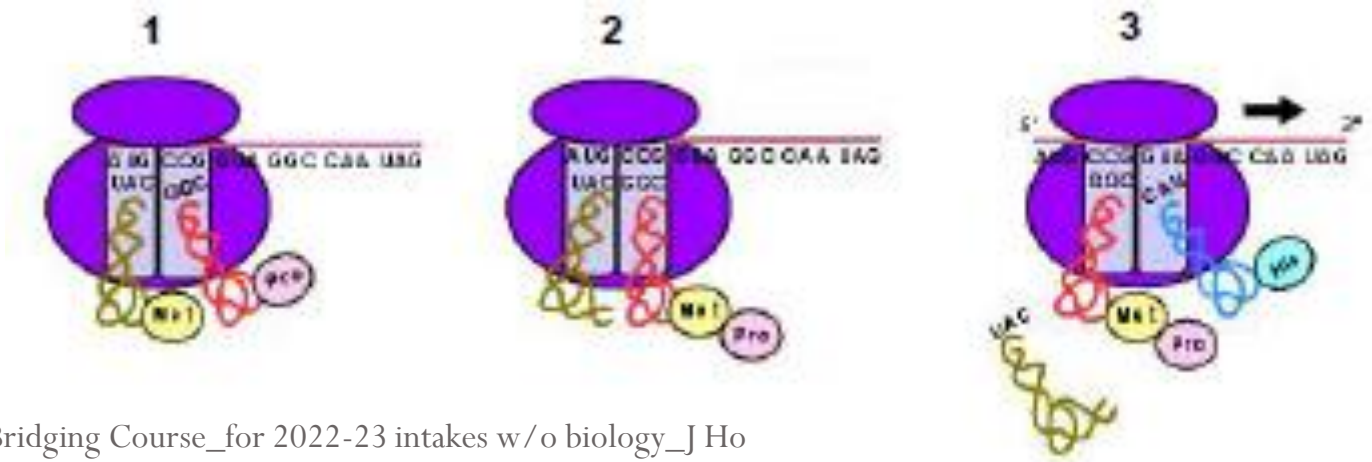
Three stage reaction cycle that add amino acids to a growing peptide

a. Binding of rRNA to A site

b. Formation of peptide bond

- Amino acid/peptide on P site tRNA attaches to the amino acid on the A site tRNA

c. P site tRNA leaves and the ribosome moves down 3 nucleotides

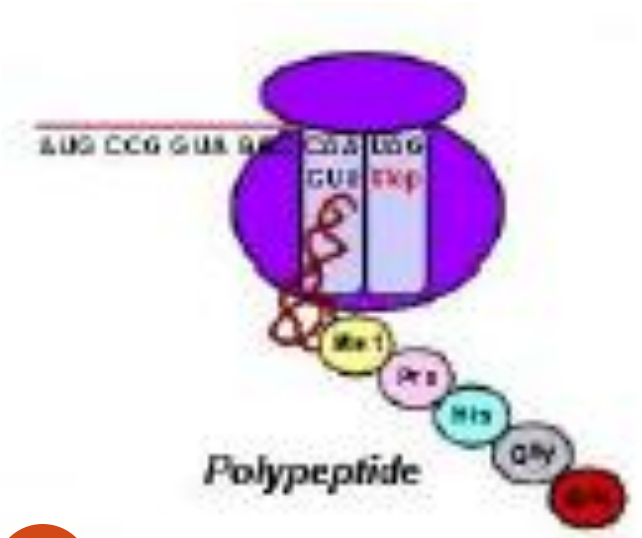


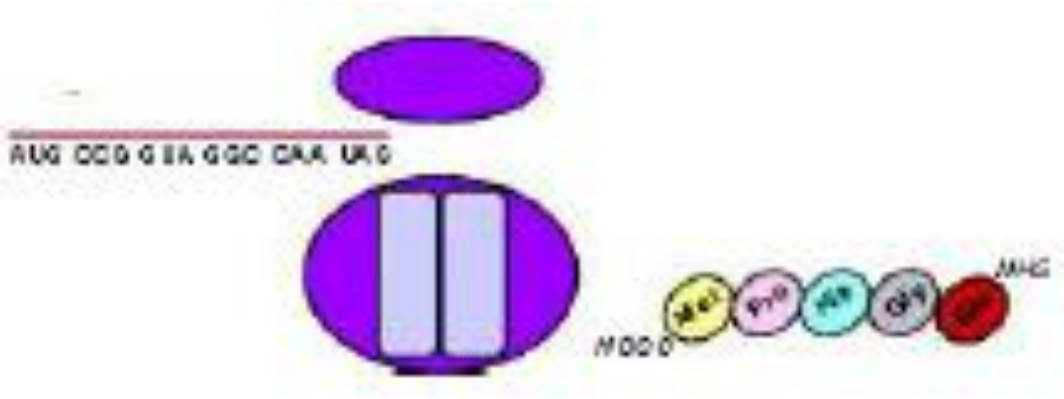
Translation: code on mRNA is read to make protein

3. Termination

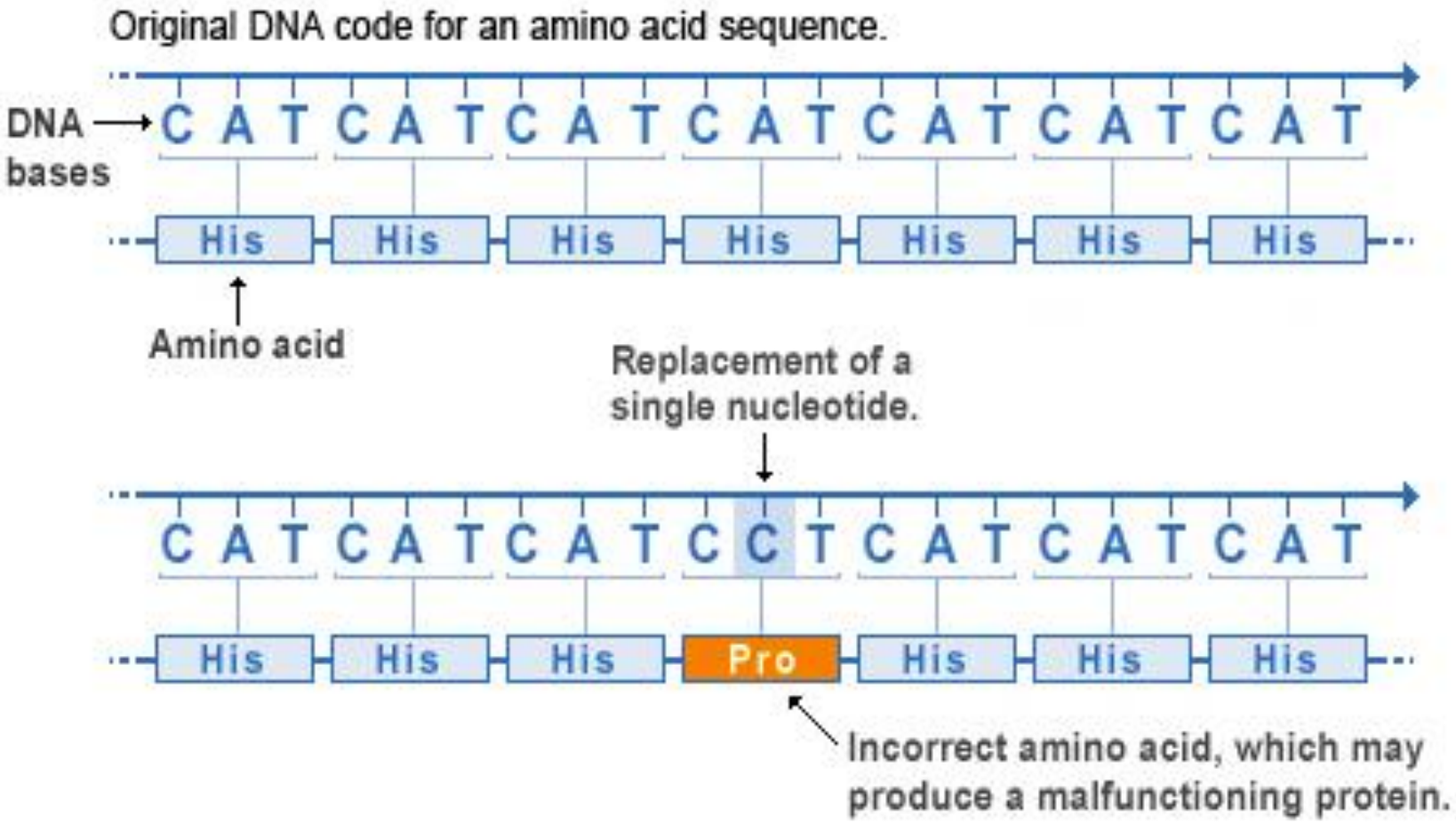
Occurs at stop site (3 stop codons – UAA, UGA, UAG) as there is no tRNA for these codons

a. A release factor binds to the empty A site
b. The polypeptide is released from P site tRNA
c. Ribosom dissembles

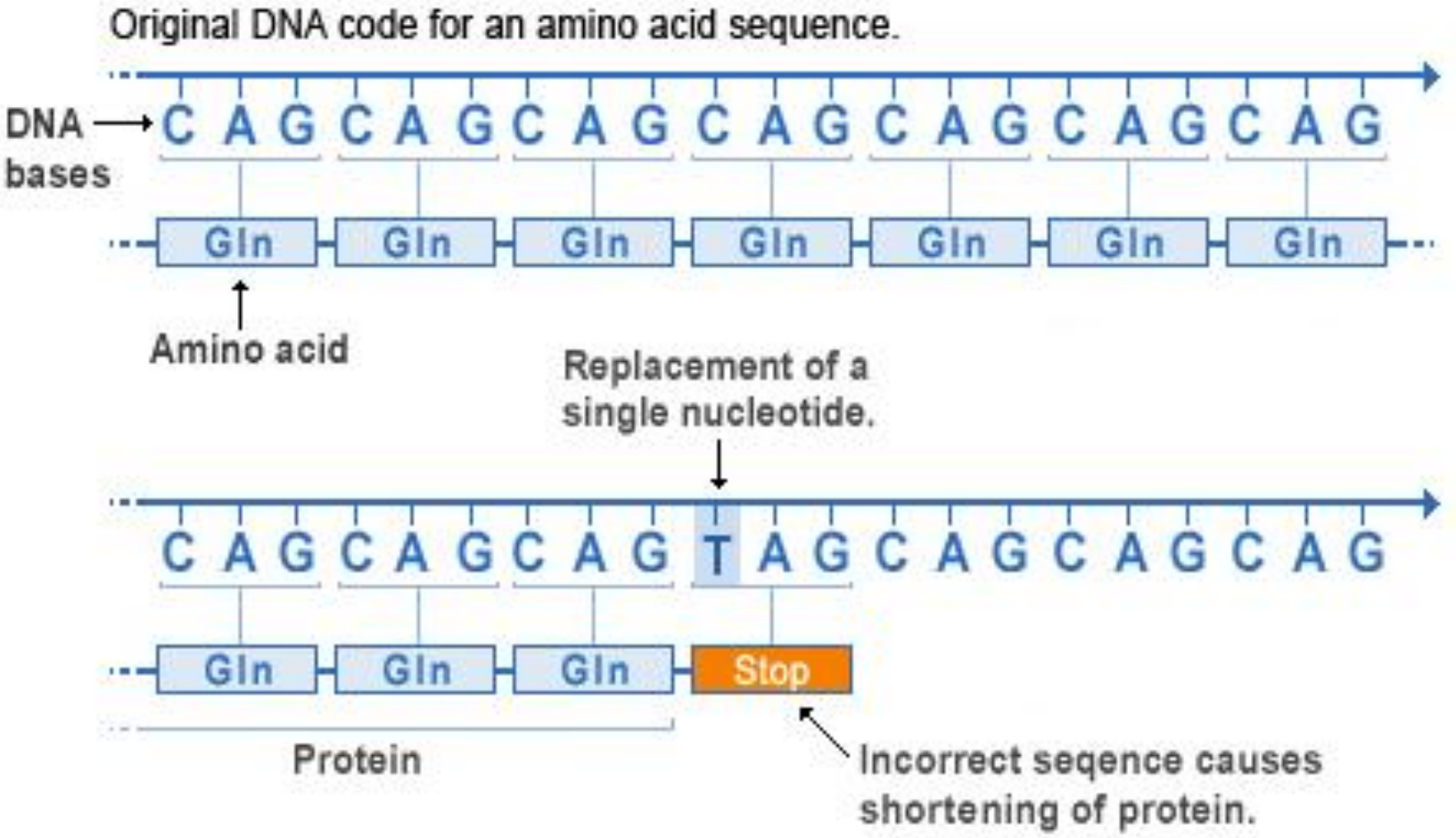




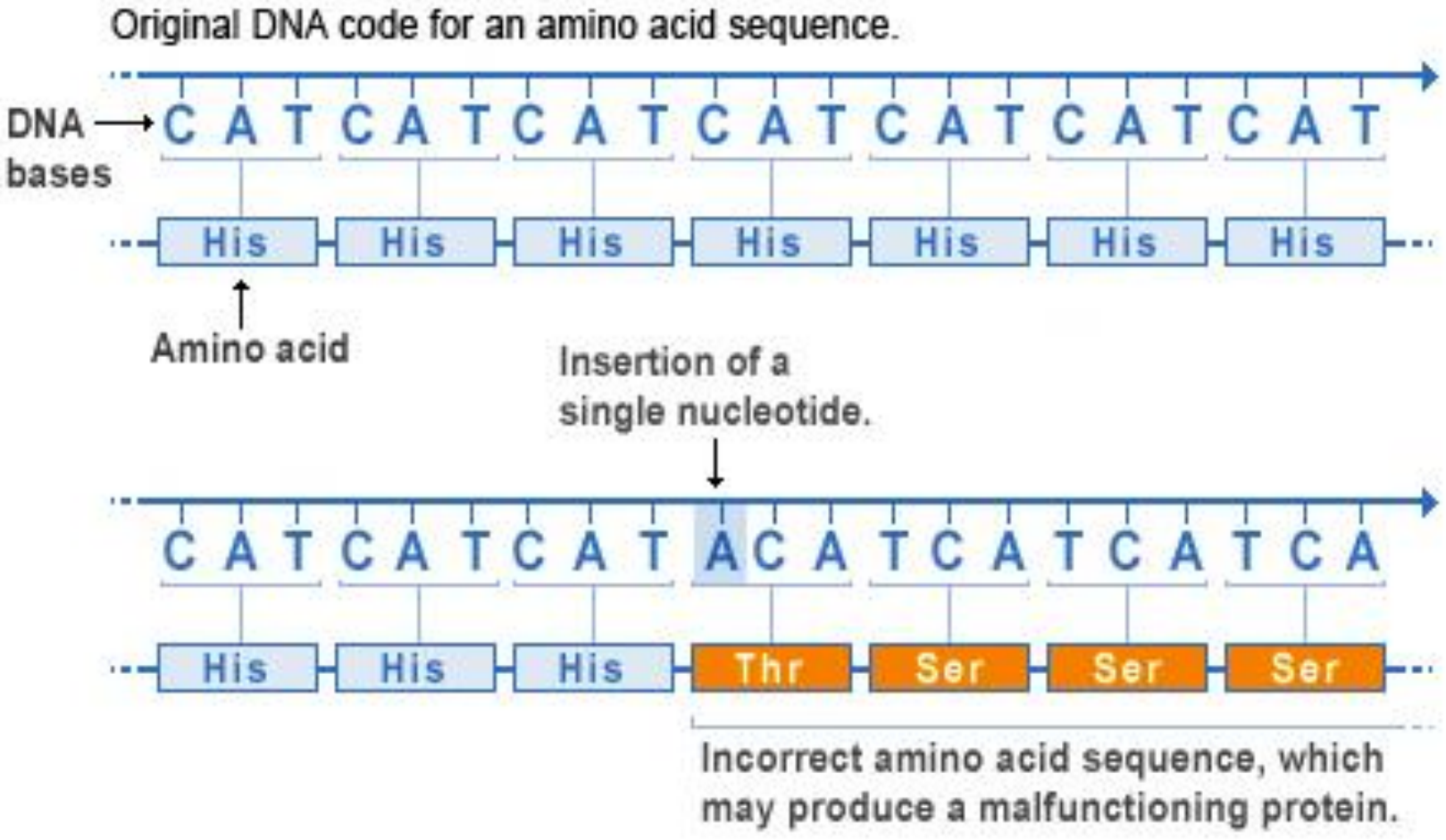
Missense mutation



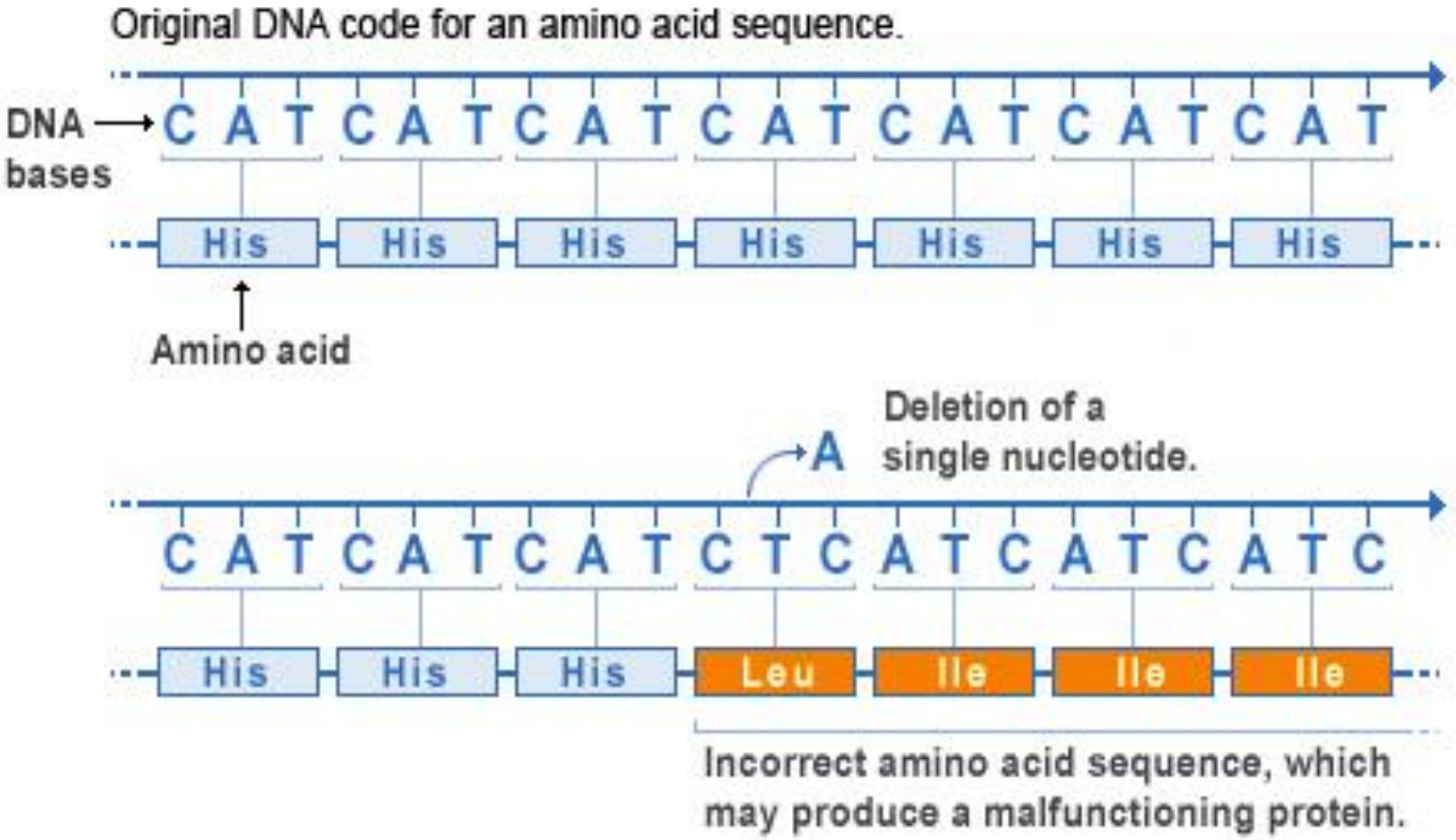
Nonsense mutation



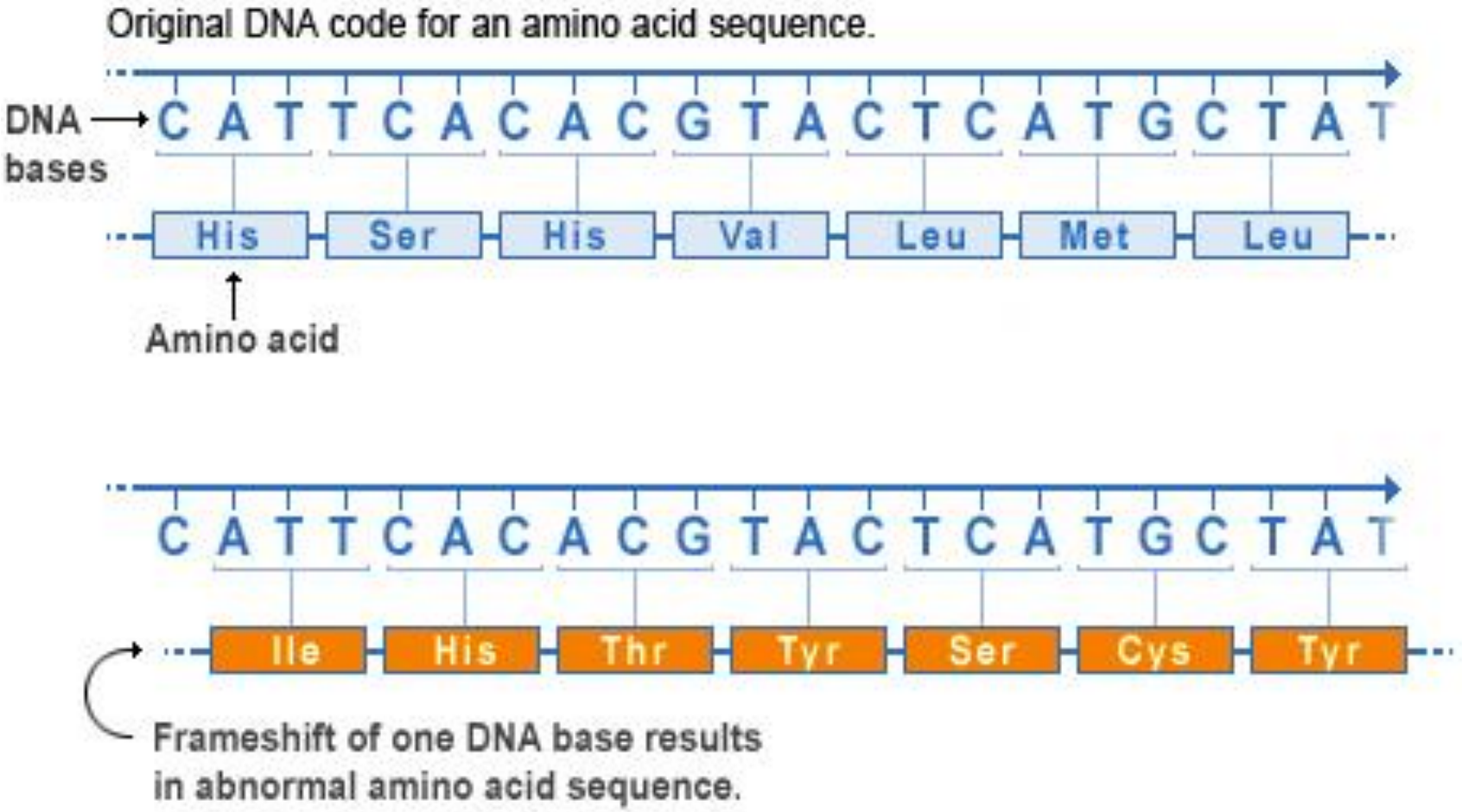
Insertion mutation



Deletion mutation

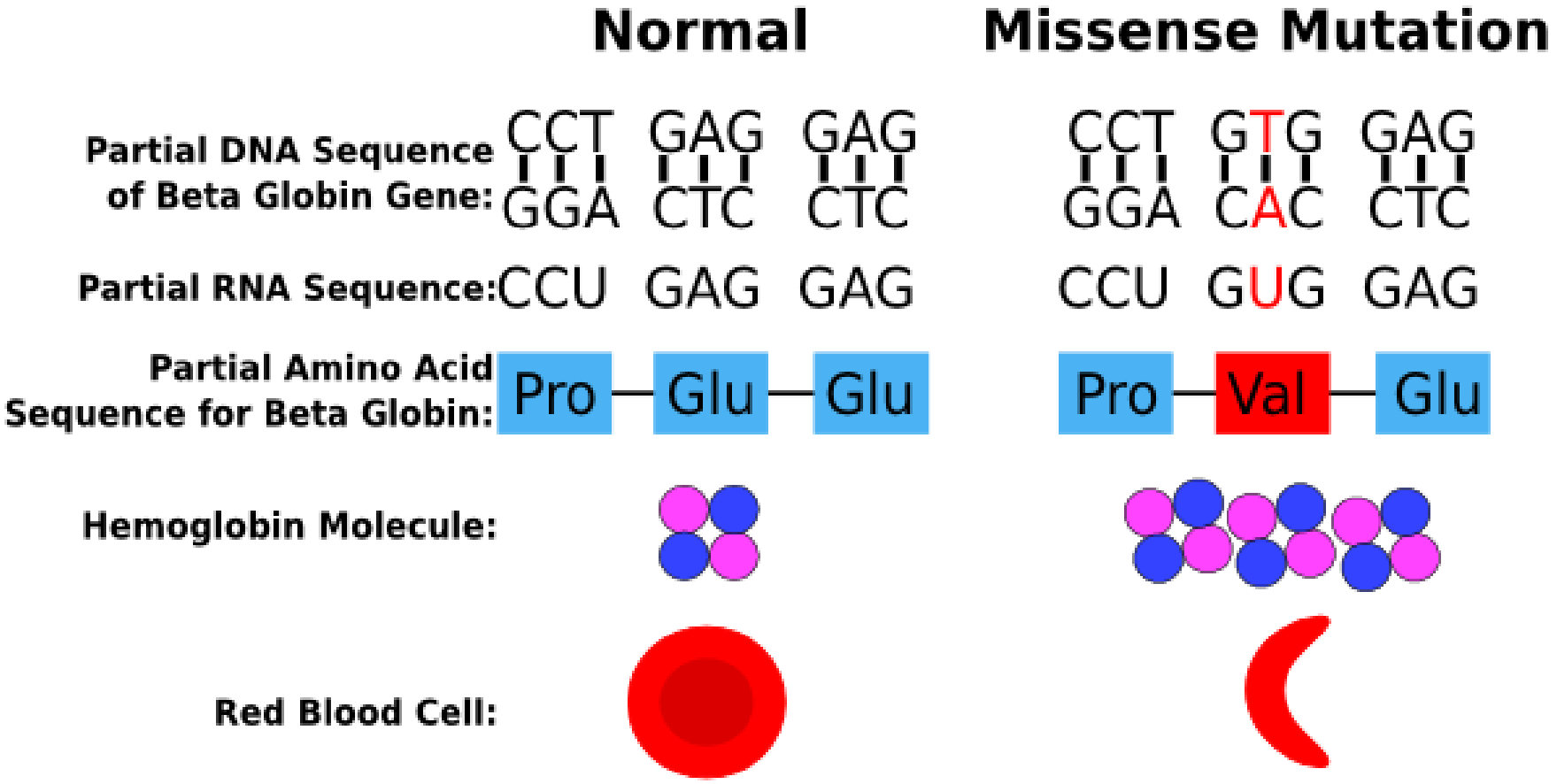


Frameshift mutation



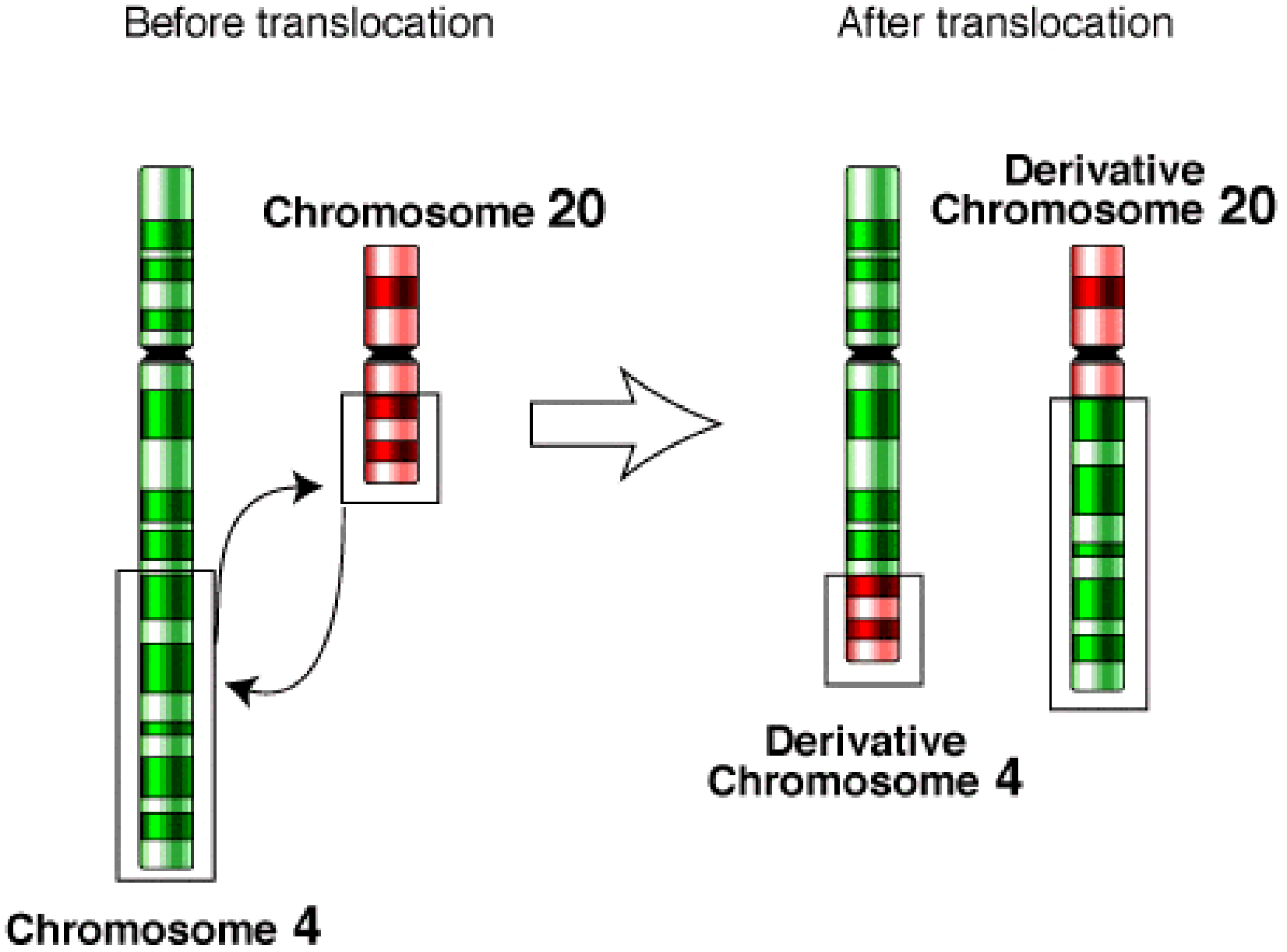
Types of mutations

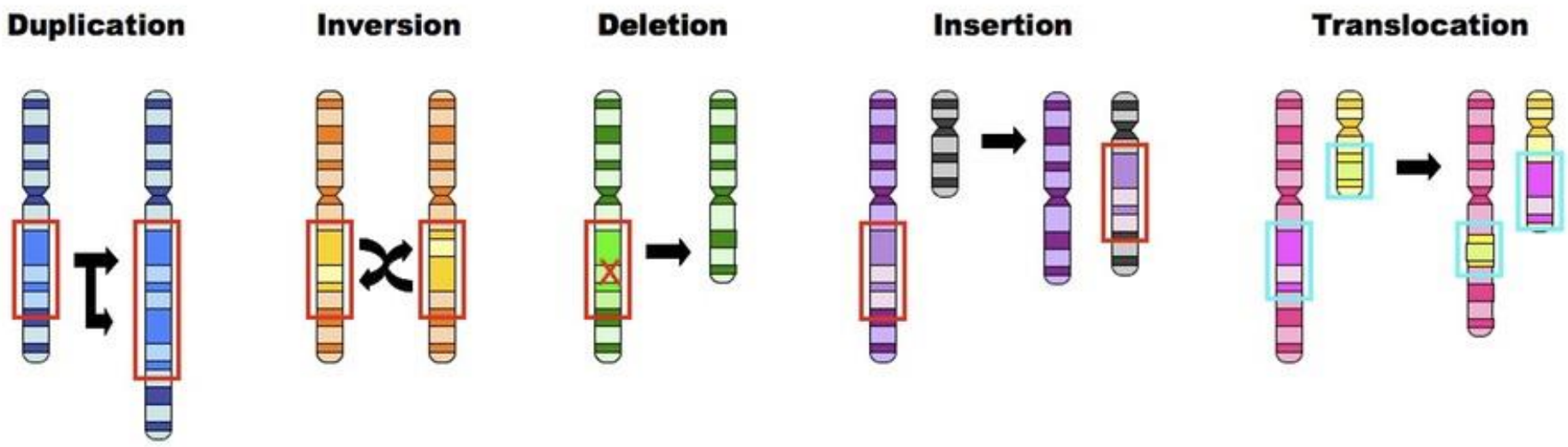
1. **Missense:** Change in amino acid
2. **Nonsense:** Change to a stop codon
3. **Insertion:** Extra base(s) inserted to the DNA
4. **Deletion:** Loss of base(s)
5. **Frameshift**: results from insertion/deletion


Normal
Missense Mutation
Partial DNA Sequence of Beta Globin Gene:
CCT GAG GAG
GGA CTC CTC
CCT GTG GAG
GGA CAC CTC
Partial RNA Sequence:
CCU GAG GAG
CCU GUG GAG
Partial Amino Acid Sequence for Beta Globin:
Pro Glu Glu
Pro Val Glu
Hemoglobin Molecule:
Red Blood Cell:

Chromosome

- The somatic (2n) and gametic (n) chromosome numbers of a species ordinarily remain constant.
- This is due to the extremely precise mitotic and meiotic cell division.
- Somatic cells of a diploid species contain two copies of each chromosome, which are called homologous chromosome.
- Their gametes, therefore contain only one copy of each chromosome, that is they contain one chromosome complement or genome.
- Each chromosome of a genome contains a definite numbers and kinds of genes, which are arranged in a definite sequence.


Before translocation
After translocation
Chromosome 20
Derivative Chromosome 20
Derivative Chromosome 4
Chromosome 4


Duplication
Inversion
Deletion
Insertion
Translocation

- Mutations in DNA can be caused by environmental agents, such as UV light and other ionizing radiations, chemicals, chemotherapeutic agents
- Variation in chromosomal number or structure do arise in nature by spontaneous mutations.

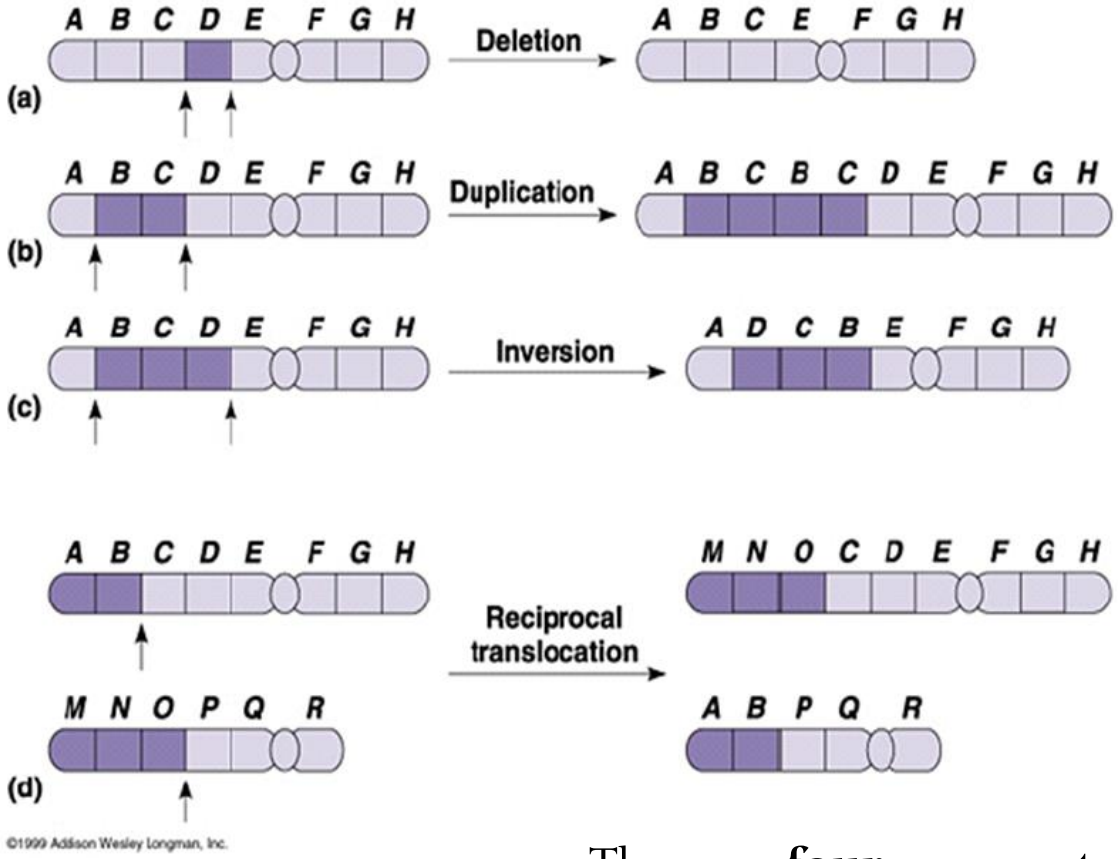
Chromosomal Aberrations

Chromosomal Aberrations

- Chromosomal aberration may be grouped into two broad classes:
  1. Structural
  2. Numerical

Structural Chromosomal Aberrations

- Chromosome structure variations result from chromosome breakage.
- Broken chromosomes tend to re-join; if there is more than one break, rejoining occurs at random and not necessarily with the correct ends.
- The result is structural changes in the chromosomes.
- Chromosome breakage is caused by X-rays, various chemicals, and can also occur spontaneously.



Structural aberrations of chromosomes

There are **four** common type of structural aberrations:

(a) Deletion or Deficiency

(b) Duplication or Repeat

(c) Inversion

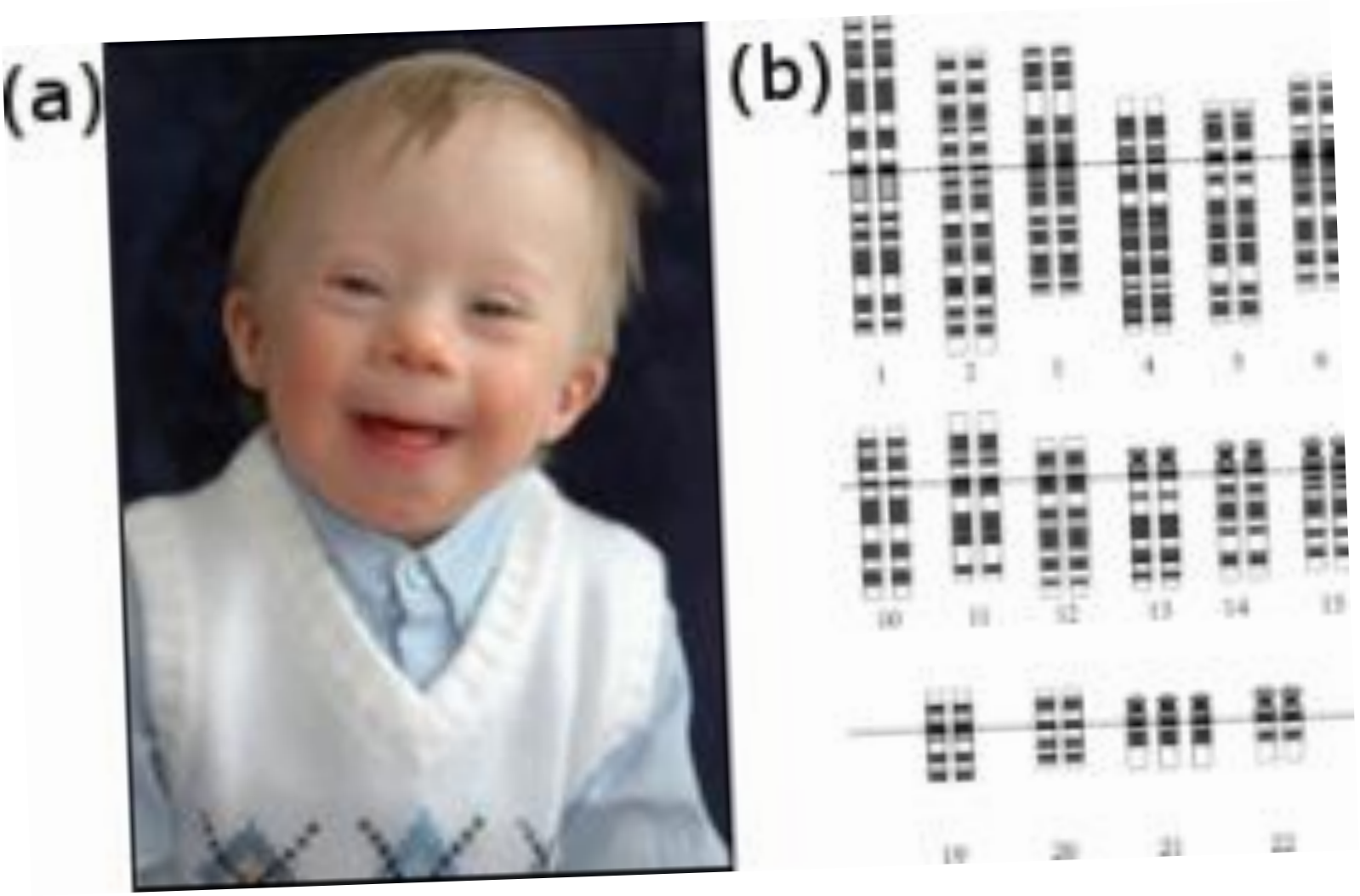
(d) Translocation

A brief description (structural aberrations)

- **Deletion** occurs when a chromosome breaks at two sites and the segment between them gets lost.
- **Duplication** means that a chromosome segment appears in two (often sequentially inserted) copies on a single homolog.
- **Inversion** occurs when a chromosome segment between two breaks is rotated 180 degrees before reinsertion.
- **Translocation** involves the exchange of chromosome segments between two nonhomologous chromosomes.

Numerical variation in chromosome

- Euploidy - Organism with one or more than one more complete set of chromosomes(applies to haploid and diploid organisms).
- Aneuploidy - Variation in the number of individual chromosomes (but not the total number of sets of chromosomes).


(a)
(b)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Vocabulary

- Base pairing
- Genes
- Nucleic acids
- Genetic code
- Transcription
- Translation
- Semi conservative DNA replication
- Mutation

Suggested reading

Maartini, F. H., Nath, J. L., & Bartholomew, E.F. (2012). *Fundamentals of anatomy and physiology*. (9th Ed.). San Francisco : Pearson/Benjamin Cummings (Chapter 3-3 to 3-4)

Fox, S. I. (2011). Human Physiology. (12th Ed.) New York : McGraw-Hill (Chapter 3.3, -3.4)

Silverthron, D. U. (2013). *Human Physiology: an integrated approach*. (6th Ed.). Upper Saddle River, N.J. ; Harlow : Pearson Education. (Chapter 4, P117-123)

http://plato.stanford.edu/entries/molecular-biology/

http://www.genome.gov/Glossary/index.cfm?id=1