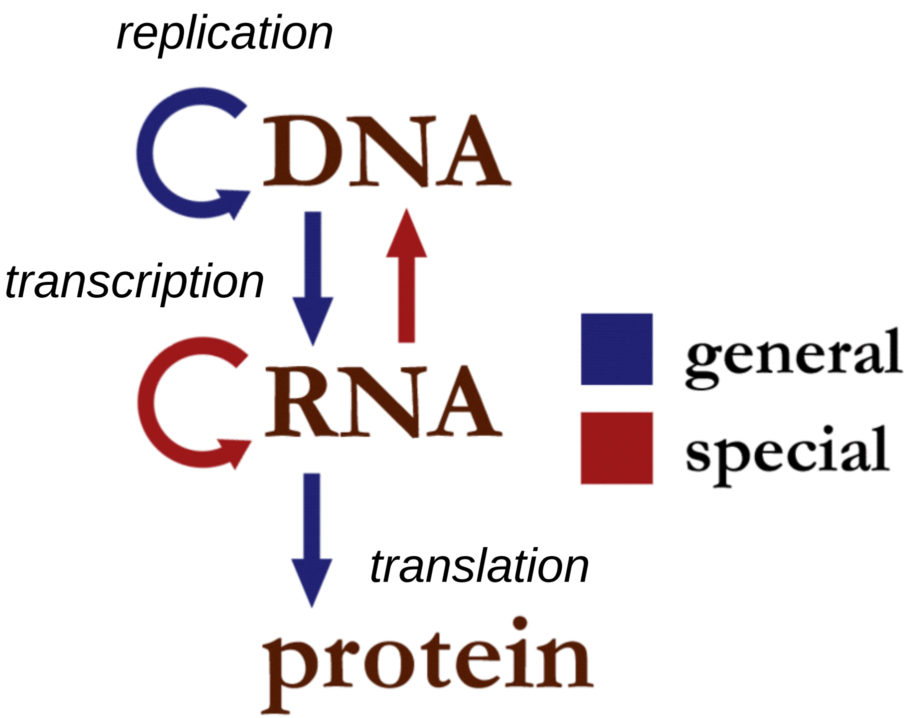
Chapter 11
Nucleic Acids and Protein Synthesis

Molecular Biology

Biomolecules are synthesized in the same order.

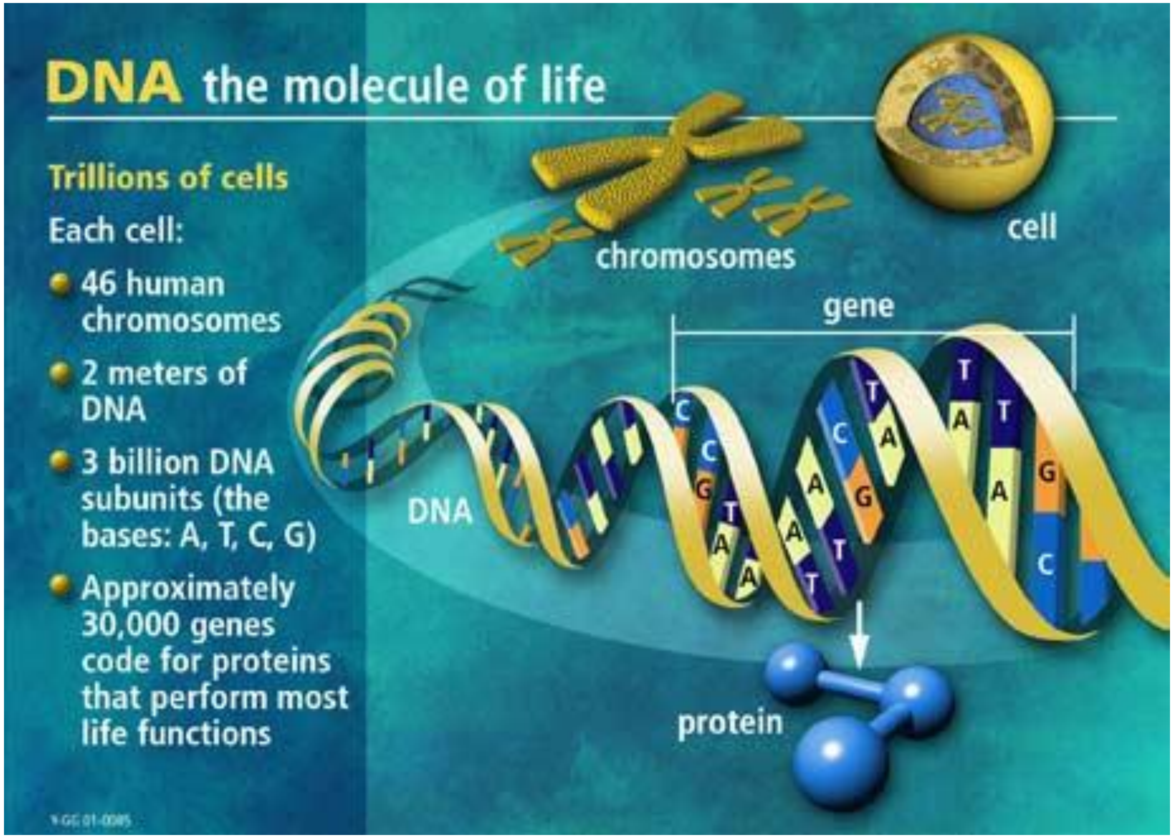


<u>general transfer</u>: occurs normally in cells

<u>special transfer</u>: occurs only in the laboratory in specific conditions

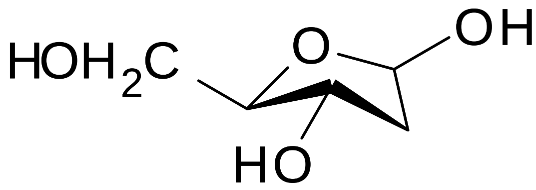
<u>unknown transfer</u>: never known to occur

The Human Genome



The human genome contains fewer than 25,000 genes.

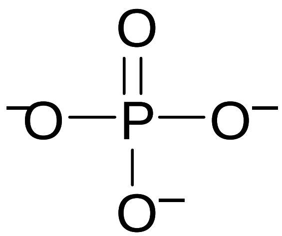
Structure of DNA



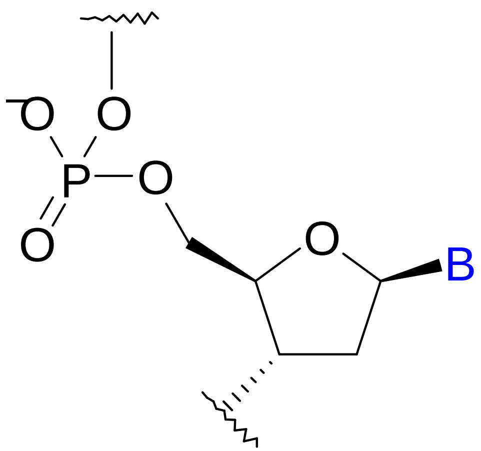
deoxyribose

The structure of DNA was not really understood until about 1950.

The backbone of DNA is linked through alternating
phosphate ester – deoxyribose – base.

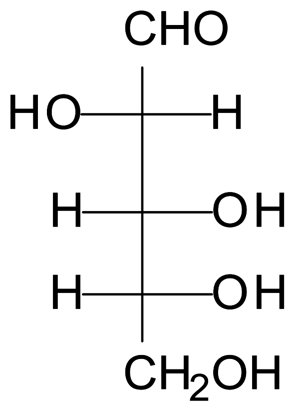


phosphate ester

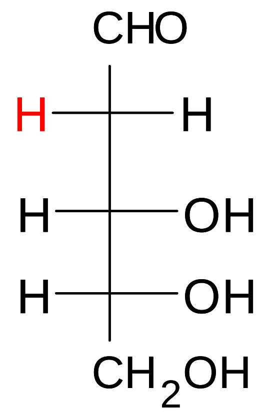


Deoxyribose

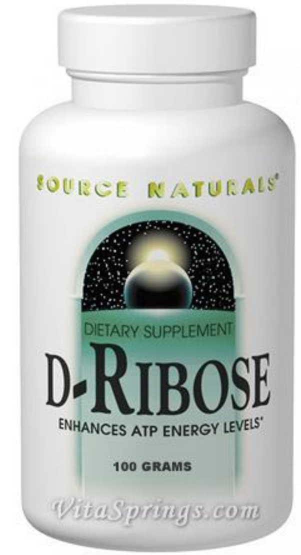
Derived from D-ribose.



D-ribose

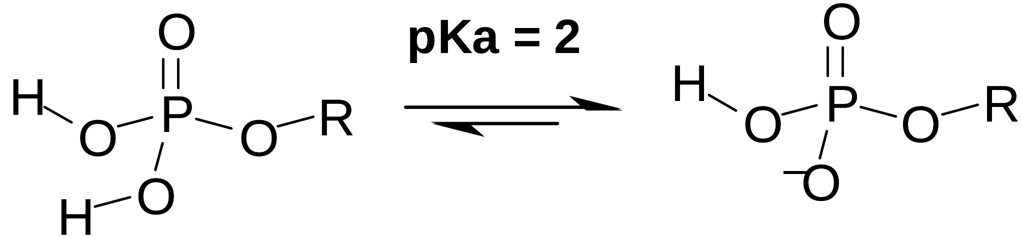


deoxyribose



D-ribose serves as the backbone for both DNA and RNA.
D-ribose has been sold as a muscle-building dietary supplement.

Phosphate Ester



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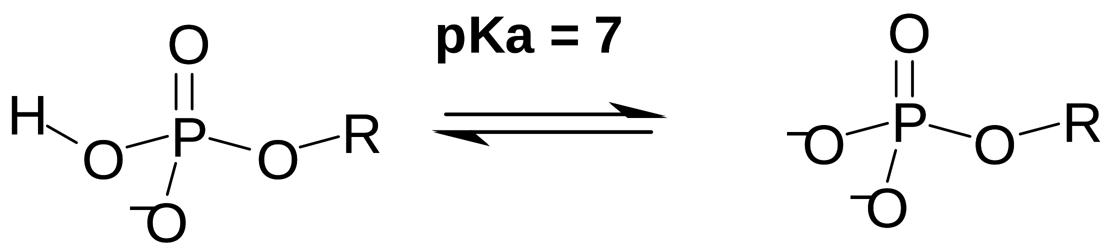
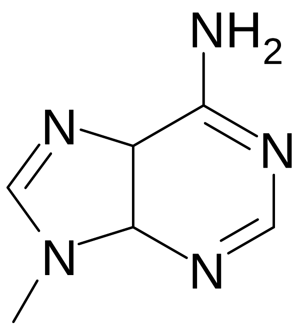


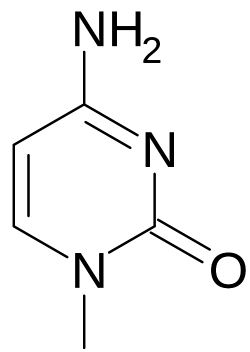
1 : 1

The phosphate ester is derived from phosphoric acid (H_3PO_4).

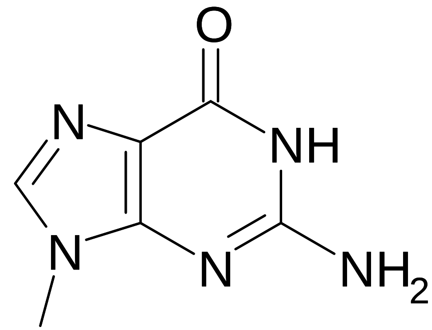
The Four Bases



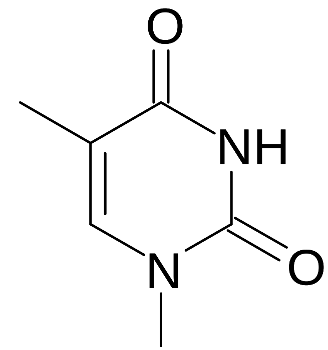
adenine



cytosine



guanine



thymine

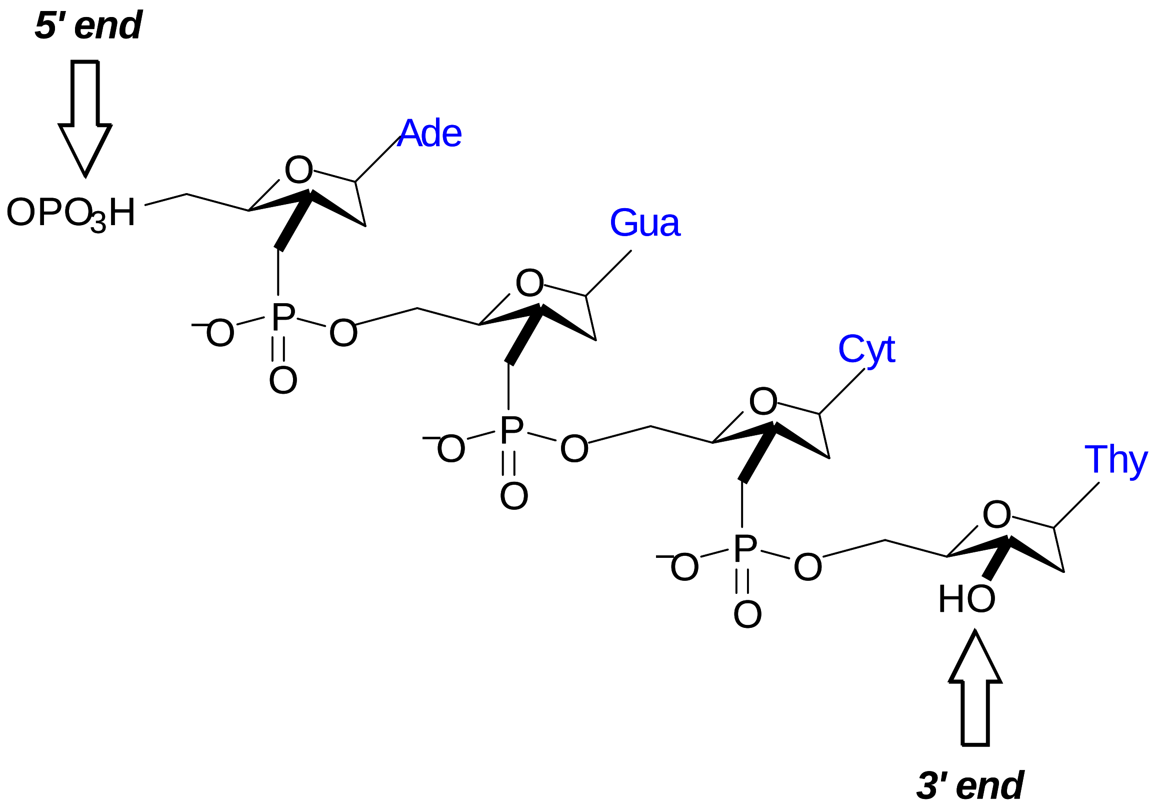
Usually referred to by their 1-letter abbreviations (A, C, G, T, respectively).

All four can be synthesized from HCN (hydrocyanic acid), H_2CO (formaldehyde), and ultraviolet light.

DNA Chains

DNA is always read from 5’ to 3’ end.

DNA sequences are read left to right.



Secondary Structure of DNA

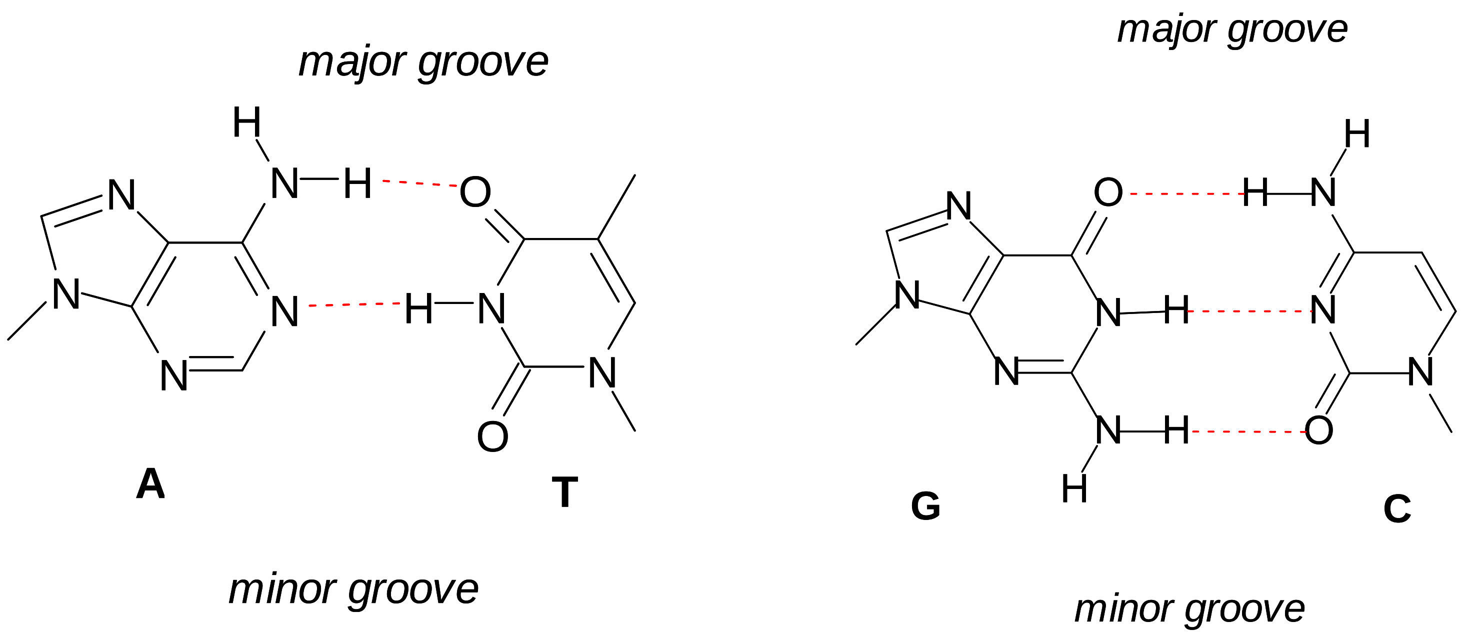
<u>primary structure:</u> determined by **covalent** bonding (alternating deoxyribose + phosphate esters)

<u>secondary structure:</u> determined by **hydrogen** bonding (Watson-Crick Base Pairs) *and* **pi-stacking.**

DNA forms a complimentary two-stranded *double helix.*

Watson-Crick Base Pairs

Nucleic acids pair to maximize hydrogen bonding.



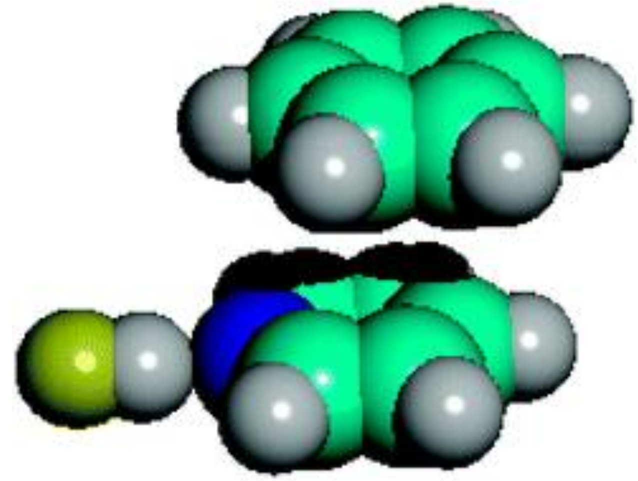
Base Pairs:

- adenine (A) + thymine (T)
- guanine (G) + cytosine (C)

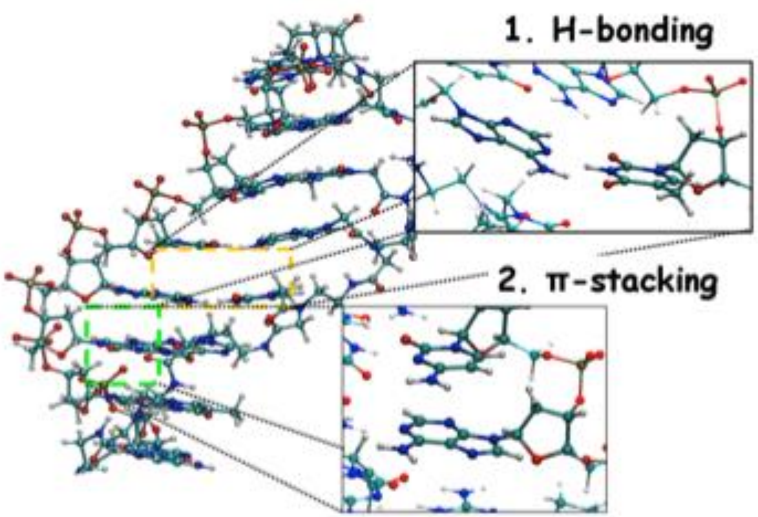
Double Helix

The two sides of DNA are *complimentary*.

5’-**AGACTG**-3’
3’-**TCTGAC**-5’



All four DNA bases are *aromatic*, meaning that they have conjugated electron sharing.



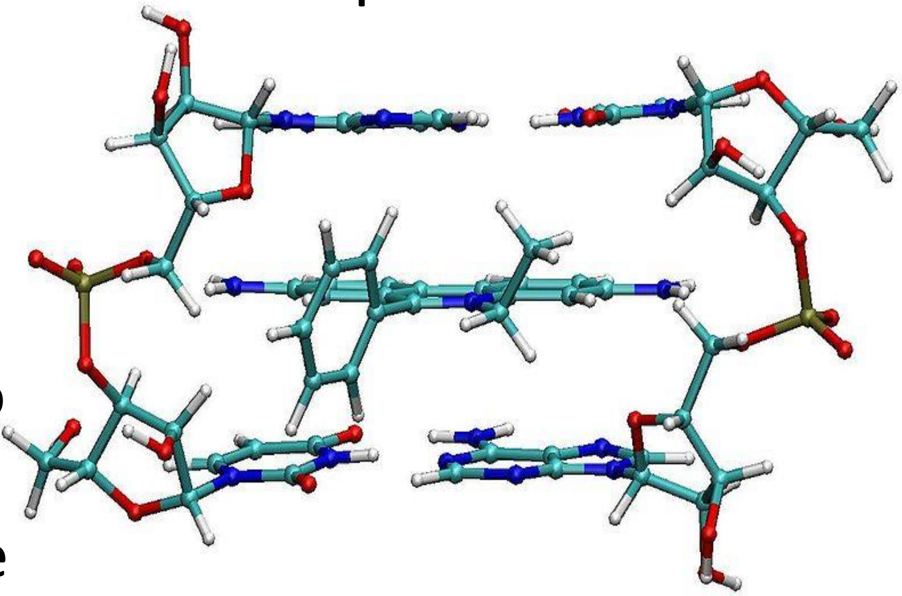
CG pairs stack better than AT pairs due to surface area and orientation.

Intercalation

<u>intercalation</u>: cationic, aromatic, planar molecules force the strands of the double helix to unwind just enough to fit between the base pairs.

This can cause:

- instability of the double helix.
- structural changes to the primary structure of DNA.
- inhibition of replication due to blocking.
- covalent bonding between the DNA strands.

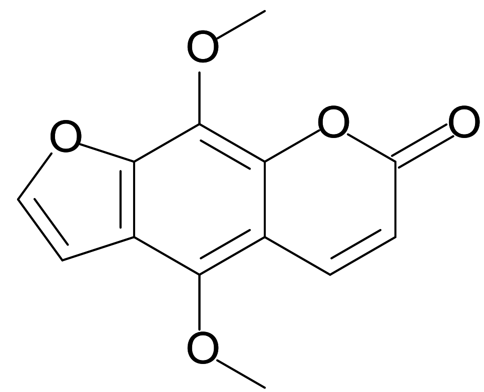


Ethidium bromide: fluorescent intercalculator used to “tag” DNA/RNA strands

The Case of the Limes

Persian limes are larger, seedless, and have a longer shelf-life than key limes but are also rich in psoralens.

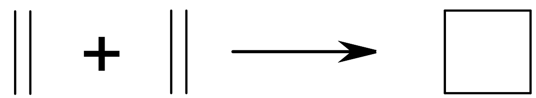
Psoralens are good intercalculators and are extremely good at absorbing ultraviolet radiation.

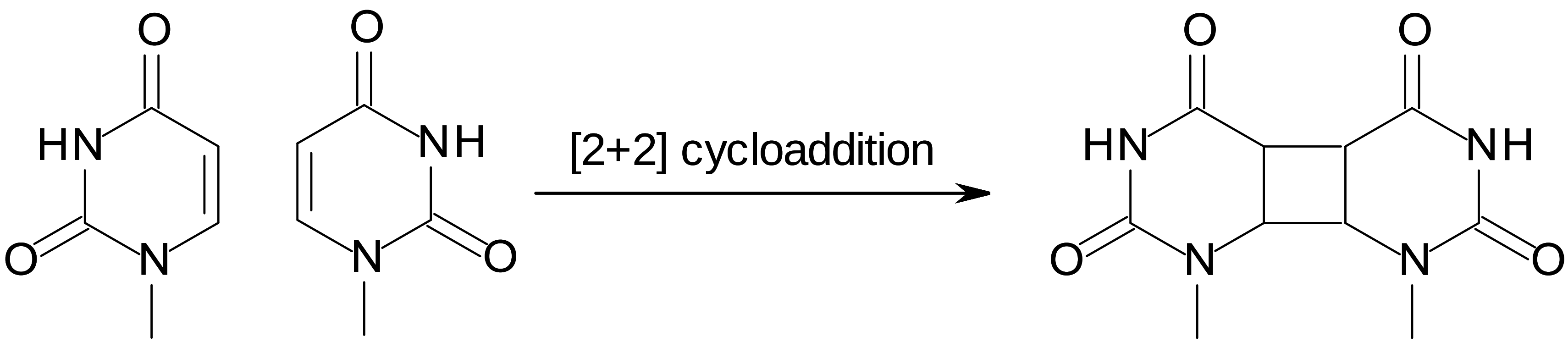


5,6-dimethoxypsoralen

Covalently Linking Thymine

2+2 cycloaddition



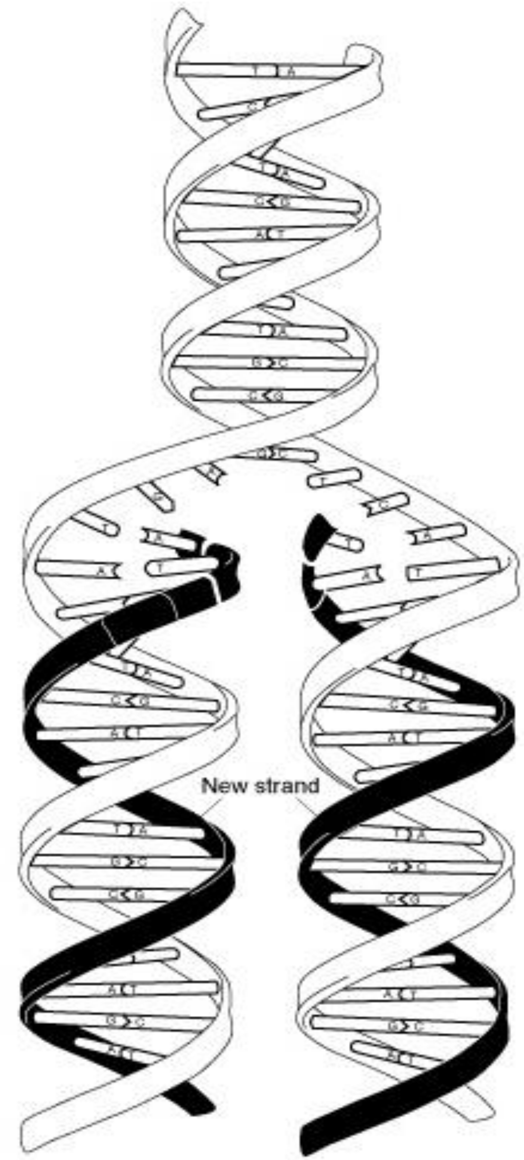


Replication

(1) DNA double helix opens, unwinds, and is held apart by proteins called **helicases**.

(2) DNA polymerase inserts into the replication fork and begins copying from the 3’ by growing a new *complimentary* chain.

(3) The new strand is released and the double helix put back together.

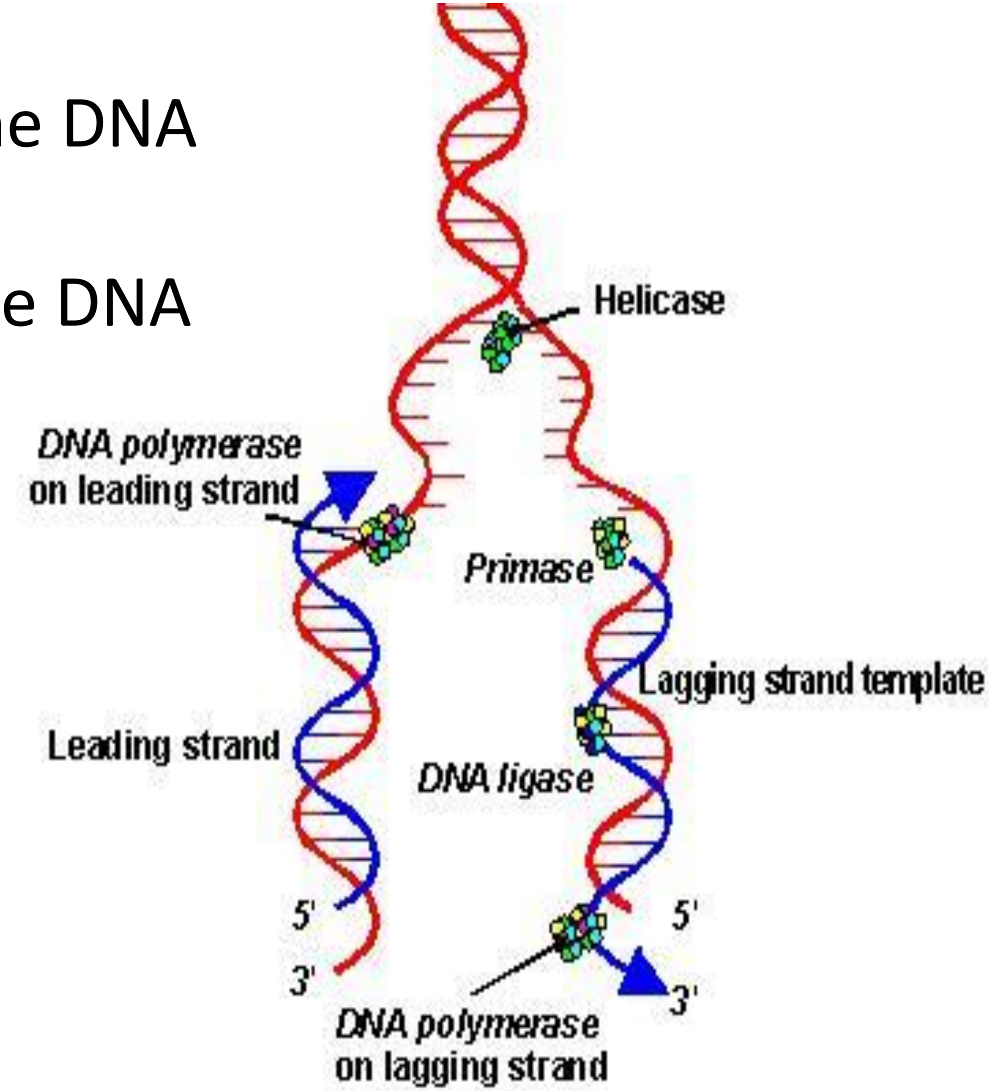


Leading and Lagging Strands

<u>Leading Strand:</u> 3' end of the DNA

<u>Lagging Strand:</u> 5' end of the DNA

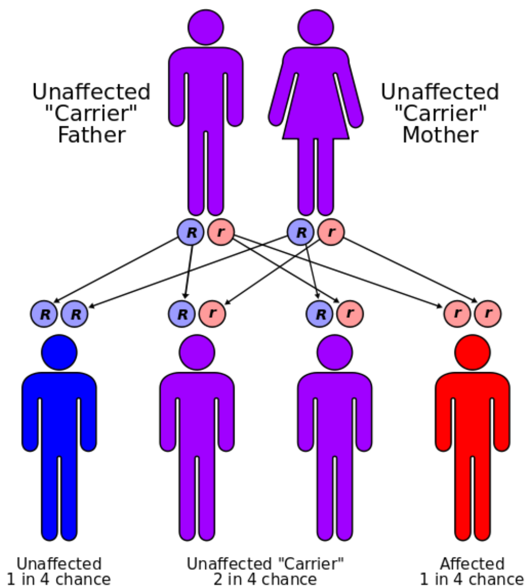
Adding to the lagging strand moving away from the helicase creates Okazaki fragments.

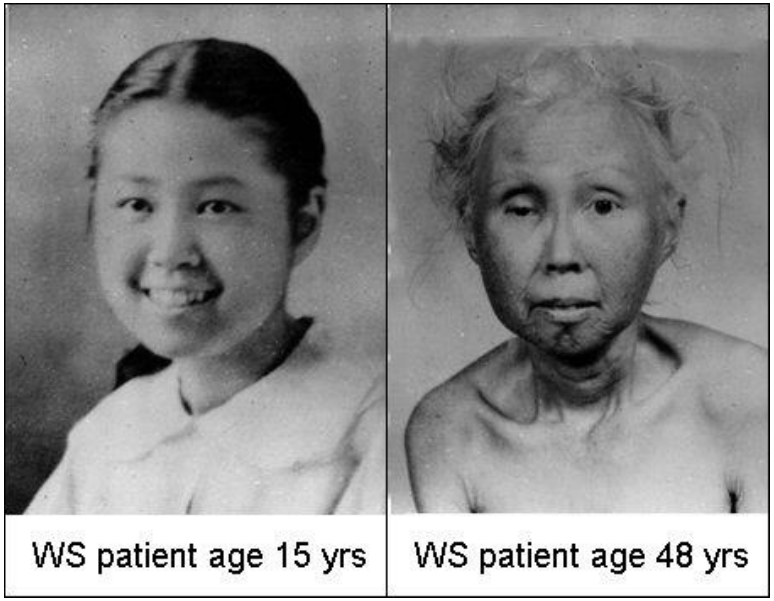


Werner's Syndrome

Small changes in DNA functions can have dramatic results

<u>Werner's Syndrome</u>: mutated DNA helicase drastically inhibits replication which leads to premature aging.





Practice Problem

Give the products after replication of the <u>leading</u> strands of the following DNA segments.

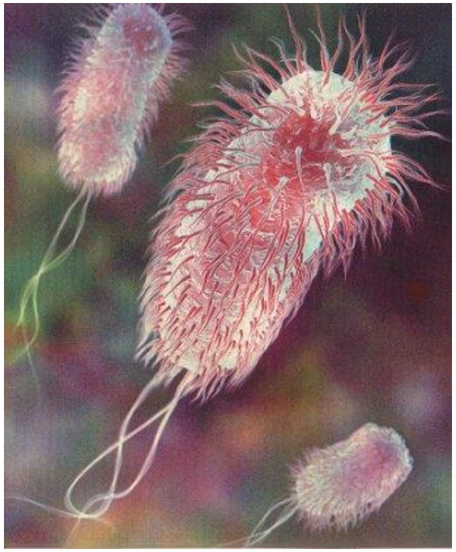
A T T C G T A G

3’-T G C C C G T G…
5’-A C G G G C A C…

Genes: From Bacteria to Human

In perspective:

- *E. coli,* a bacteria, has 4,291 genes.
- *C. elegans,* a roundworm, has about 20,000 genes.
- The human genome estimates about 23,000 genes.



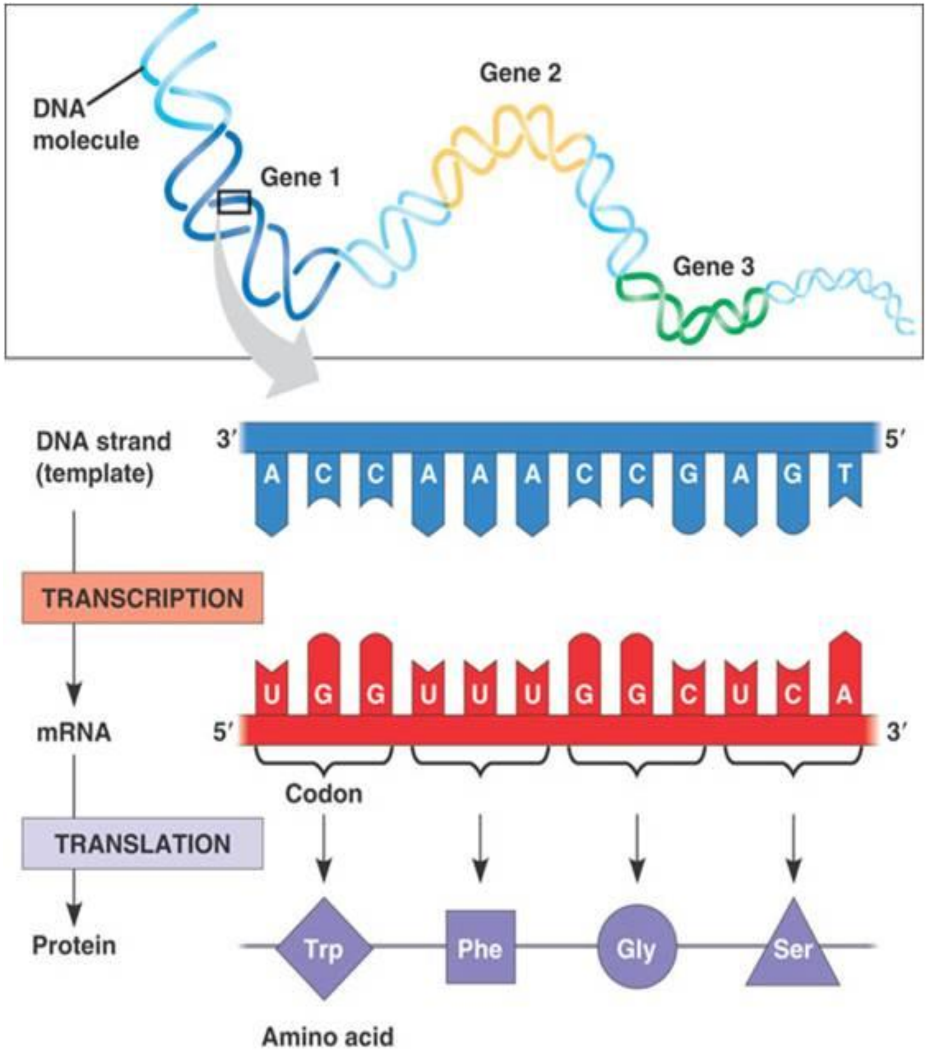
Genes: What Makes You…You?

- Genes are *hereditary*.
  - Genetic traits can be passed on between generations.

- Genes are inherently complicated.
  - The average gene consists of 3,000 bases.

- Most of the human genome still remains a mystery.
  - Humans share 99% of their genes with mice.
  - Almost 99.9% of all nucleotide bases are identical from person to person.
  - Over 50% of human genes have no known function.

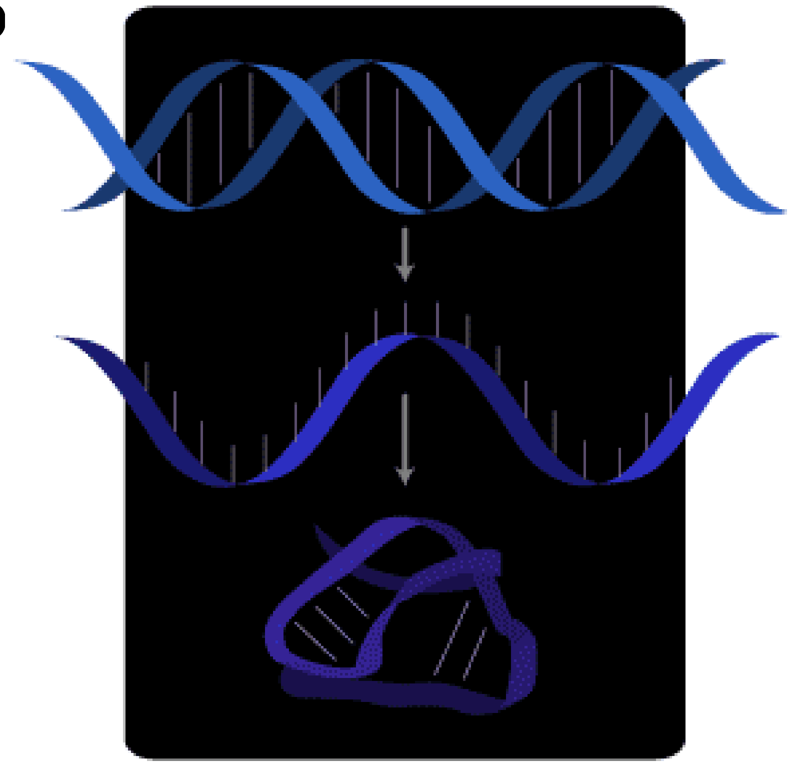
Molecular Biology



<u>Gene expression</u> is the "turning on" or activation of a gene.

Making RNA

<u>transcription</u>: DNA is recorded into a complimentary, single-stranded RNA (ribonucleic acid) molecule.



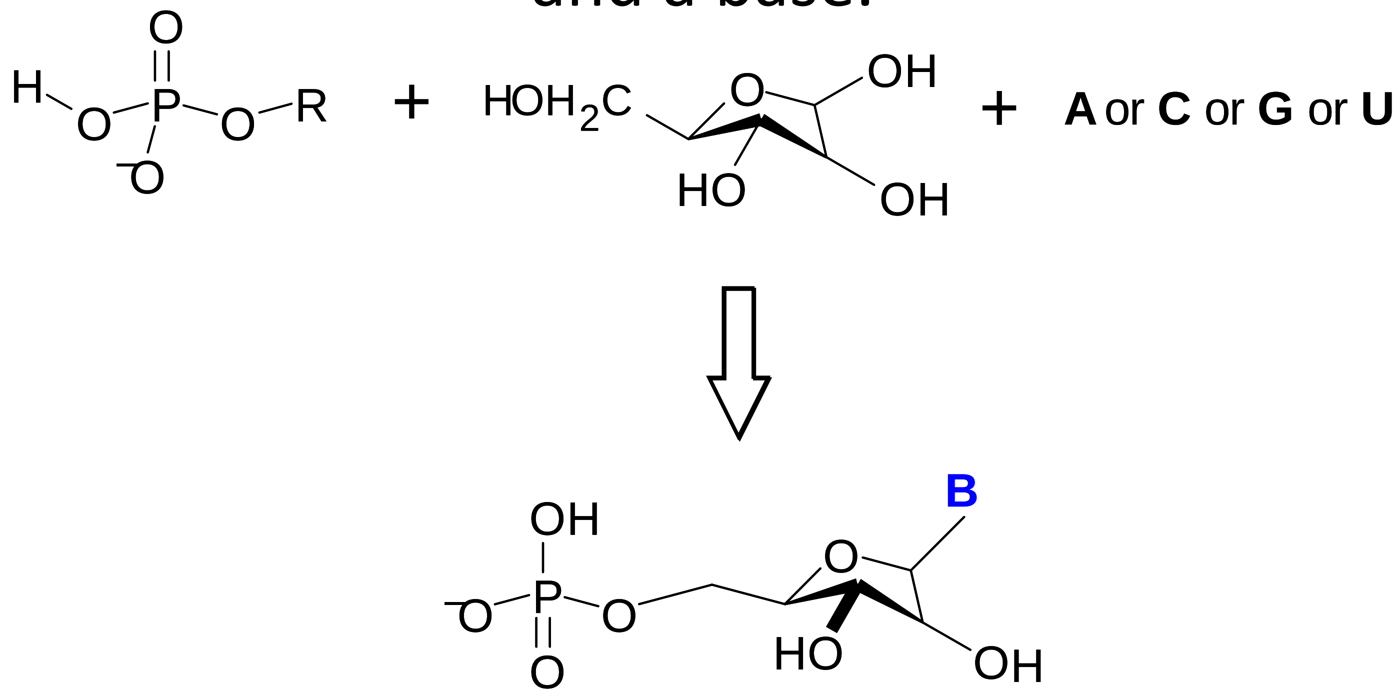
RNA is classified by its function.

Categories of RNA:

1. Messenger RNA (mRNA)
2. Transfer RNA (tRNA)
3. Ribosomal RNA (rRNA)
4. Small nuclear RNA (snRNA)
5. Micro RNA (miRNA)
6. Small Interfering RNA (siRNA)

From DNA to RNA

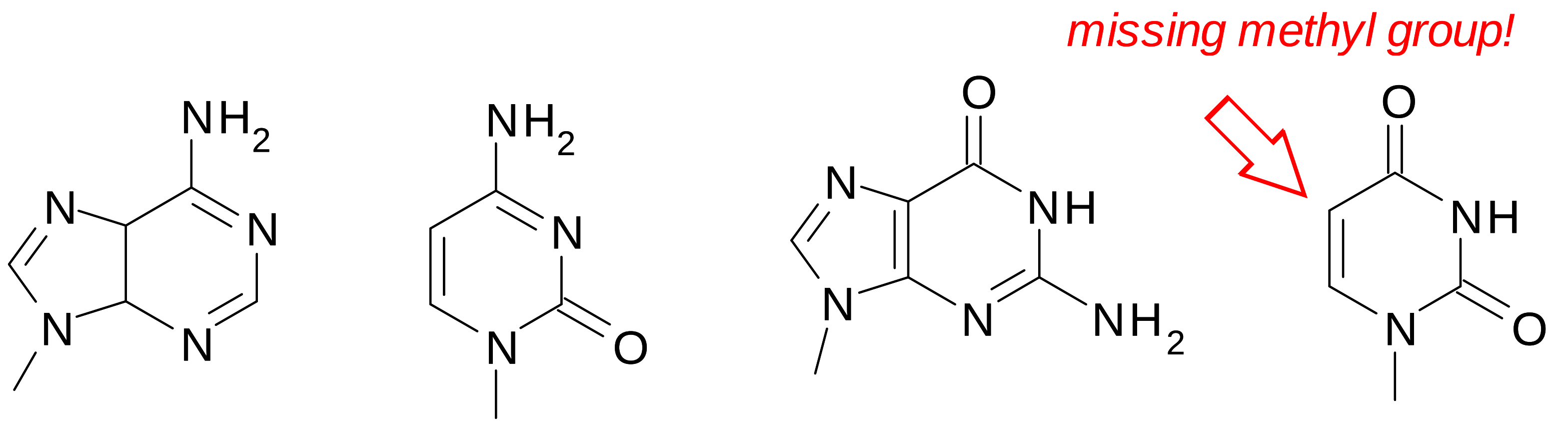
RNA contains a phosphate ester, a monosaccharide, and a base.



RNA chains together exactly like DNA with a 5’ and a 3’ end.

Differences from DNA and RNA

- RNA contains D-ribose, rather than deoxyribose.
- Thymine is replaced with uracil.

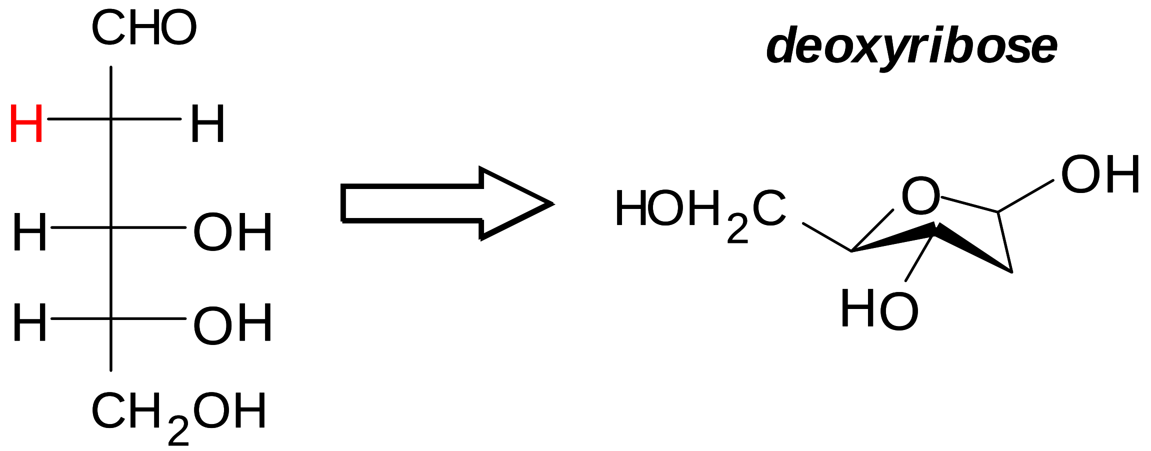


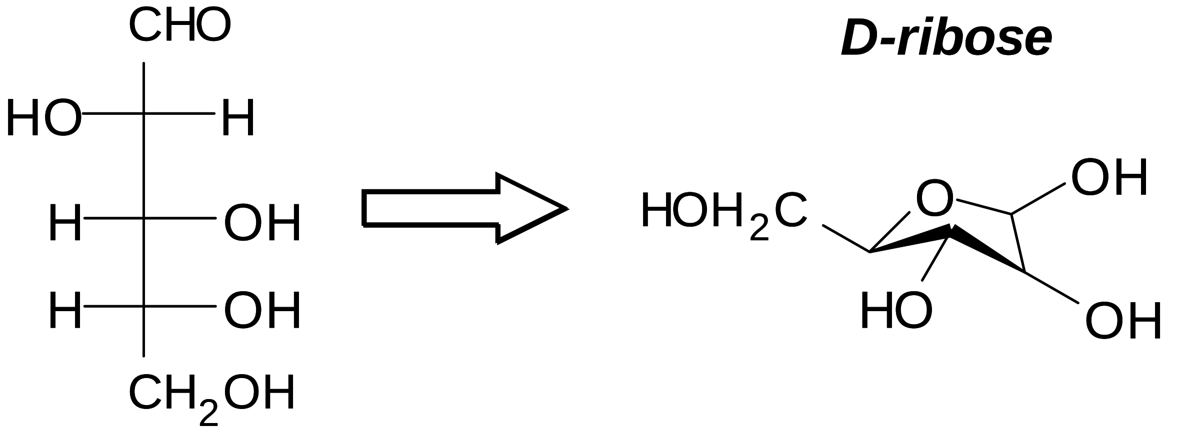
adenine ***cytosine*** ***guanine*** ***uracil***

In RNA, the base pairs are:

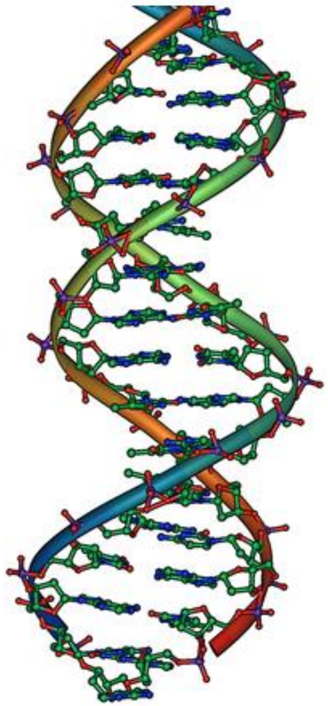
- adenine + uracil (AU)
- cytosine + guanine (CG)

Carbohydrate Linkers

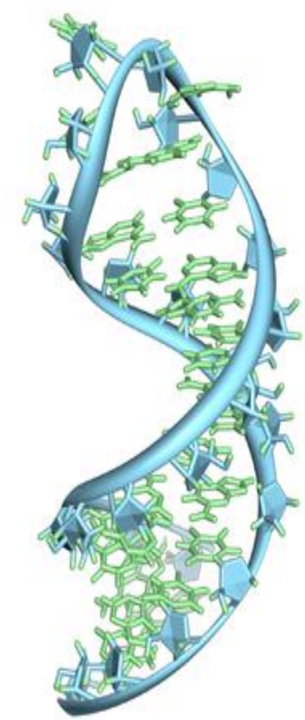




Secondary Structure of RNA



DNA is **two** strands that form a double helix.



RNA is a **single** strand that forms knots.

RNA Knots

Strands of RNA try to maximize their base pairs.

A

<u>hairpins:</u> terminal ends of the RNA strand match, but internal sections do not

B

<u>kissing complexes:</u> two separate RNA strands match a central section

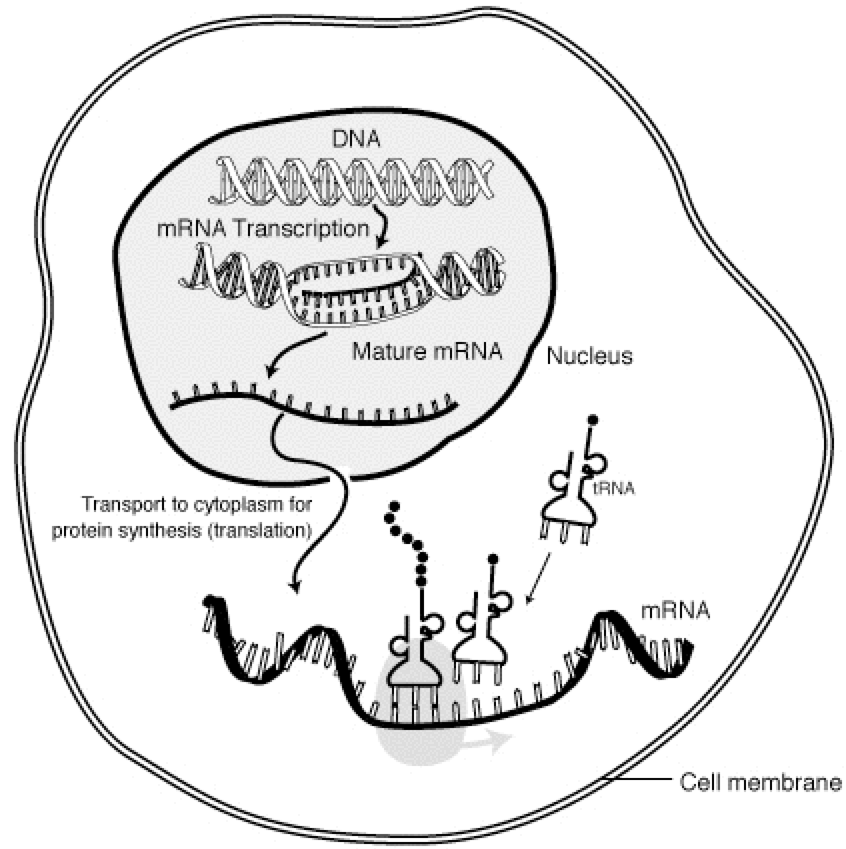
C

<u>duplexes:</u> two RNA strands matching horizontally.

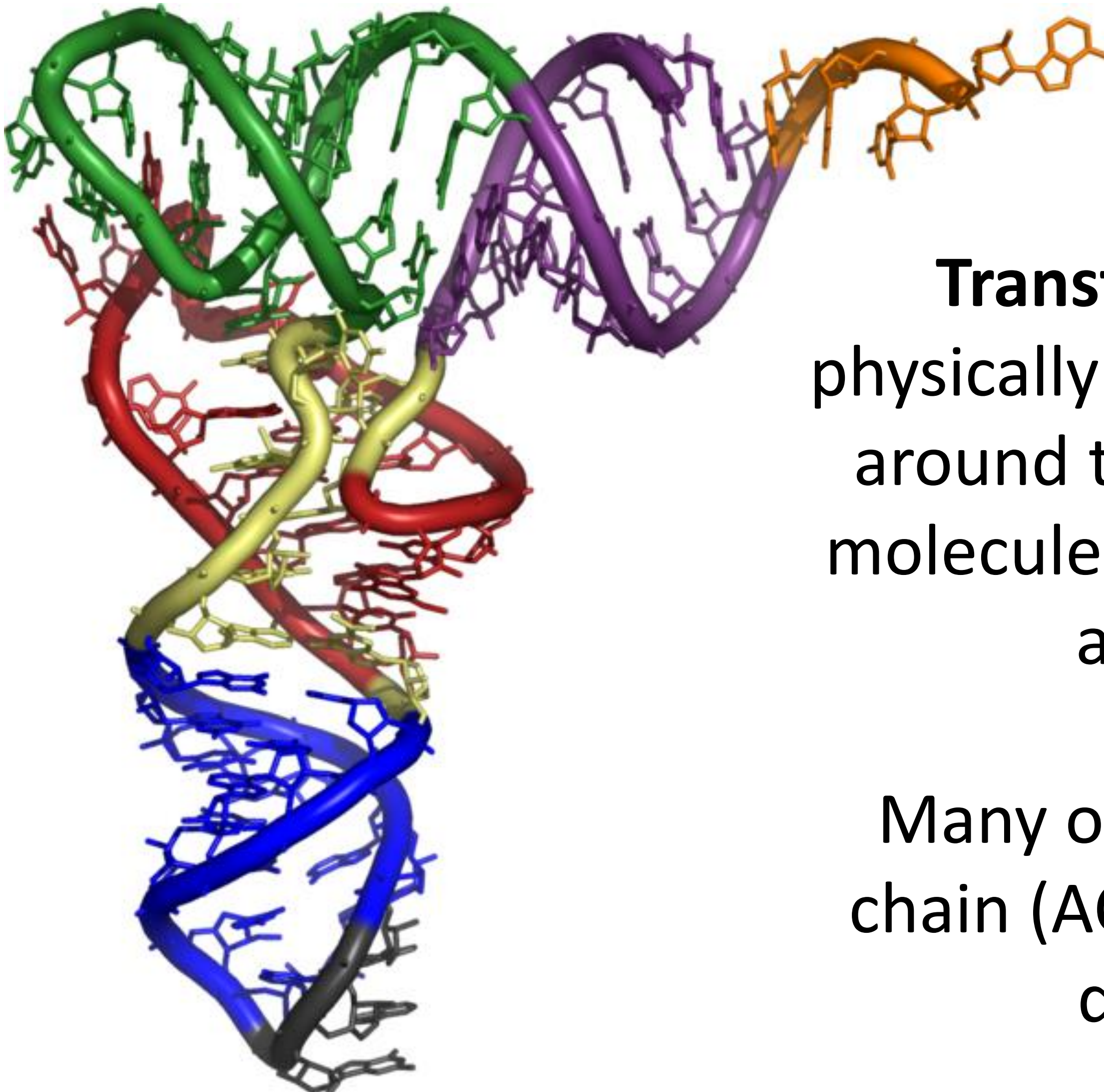
Messenger RNA (mRNA)

mRNA is translated by the ribosome to dictate the ordering of produced amino acids.

The lifespan of mRNA is incredibly short; it is only produced when needed.



Transfer RNA (tRNA)

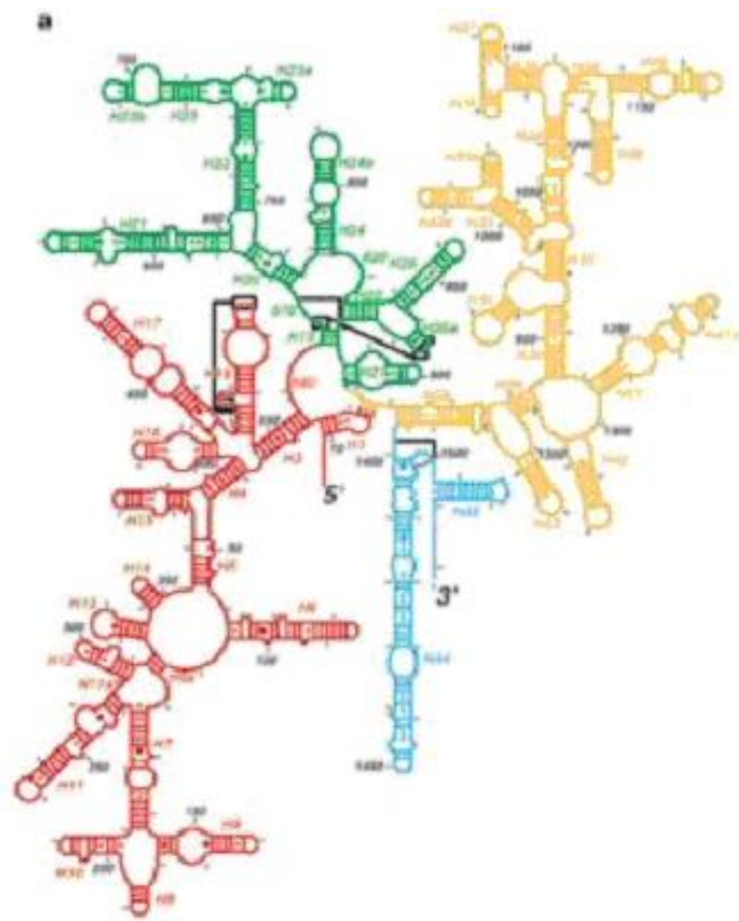


Transfer RNA (tRNA) physically moves amino acids around the cell. The tRNA molecule is individual to the amino acid.

Many of the bases in the chain (ACGU) are modified derivatives.

Ribosomal RNA (rRNA)

Ribosomal RNA (rRNA) combines with proteins to form ribosomes, the location at which other proteins can be synthesized. The molecules formed are often huge (> 1 million g/mol).



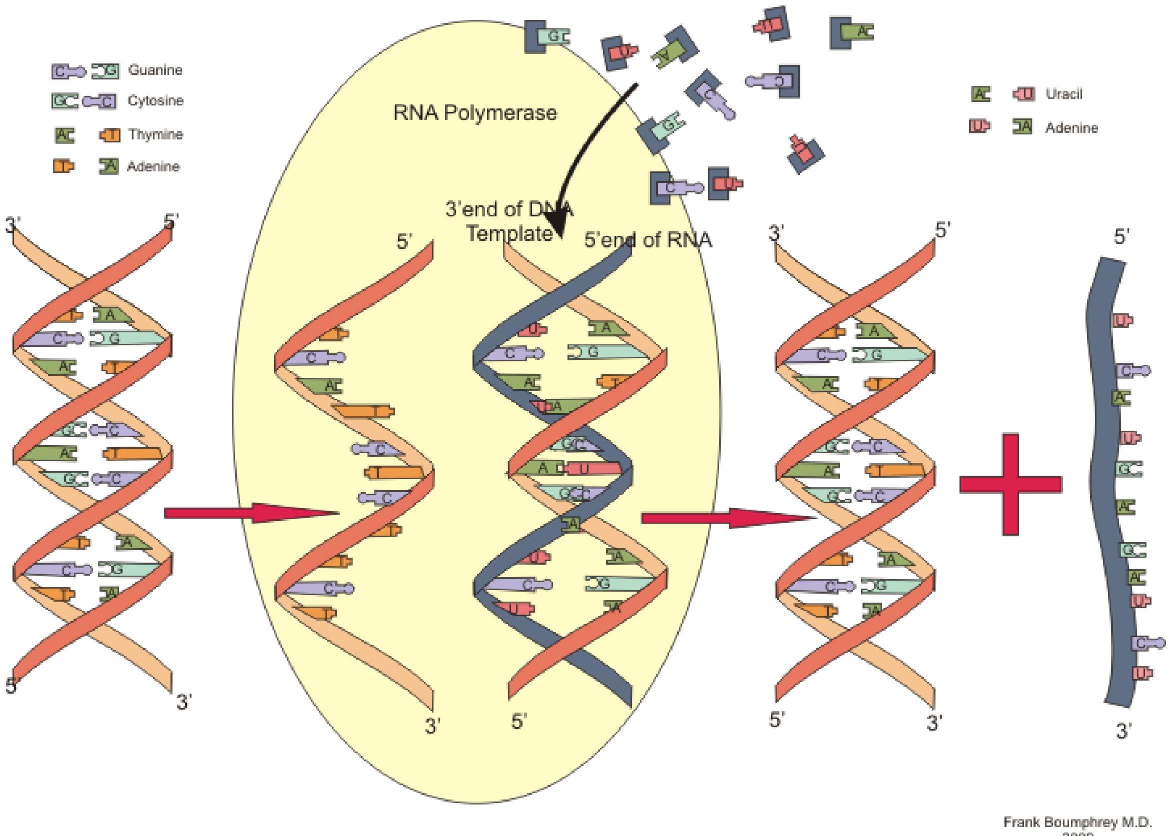
Transcription

Similar to the process of *replication*.

Initiation

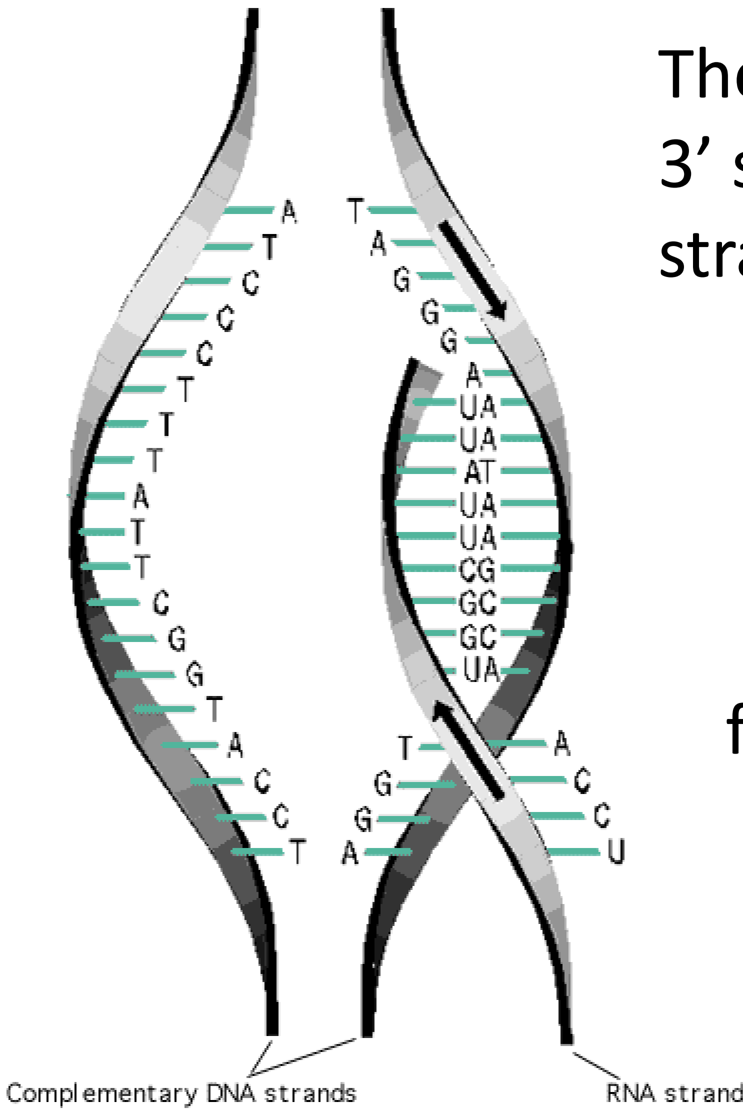
Elongation

Termination



Formation of mRNA Strand From DNA Template

Sequencing



The RNA is synthesized from the 3' side, making a *complimentary* strand.

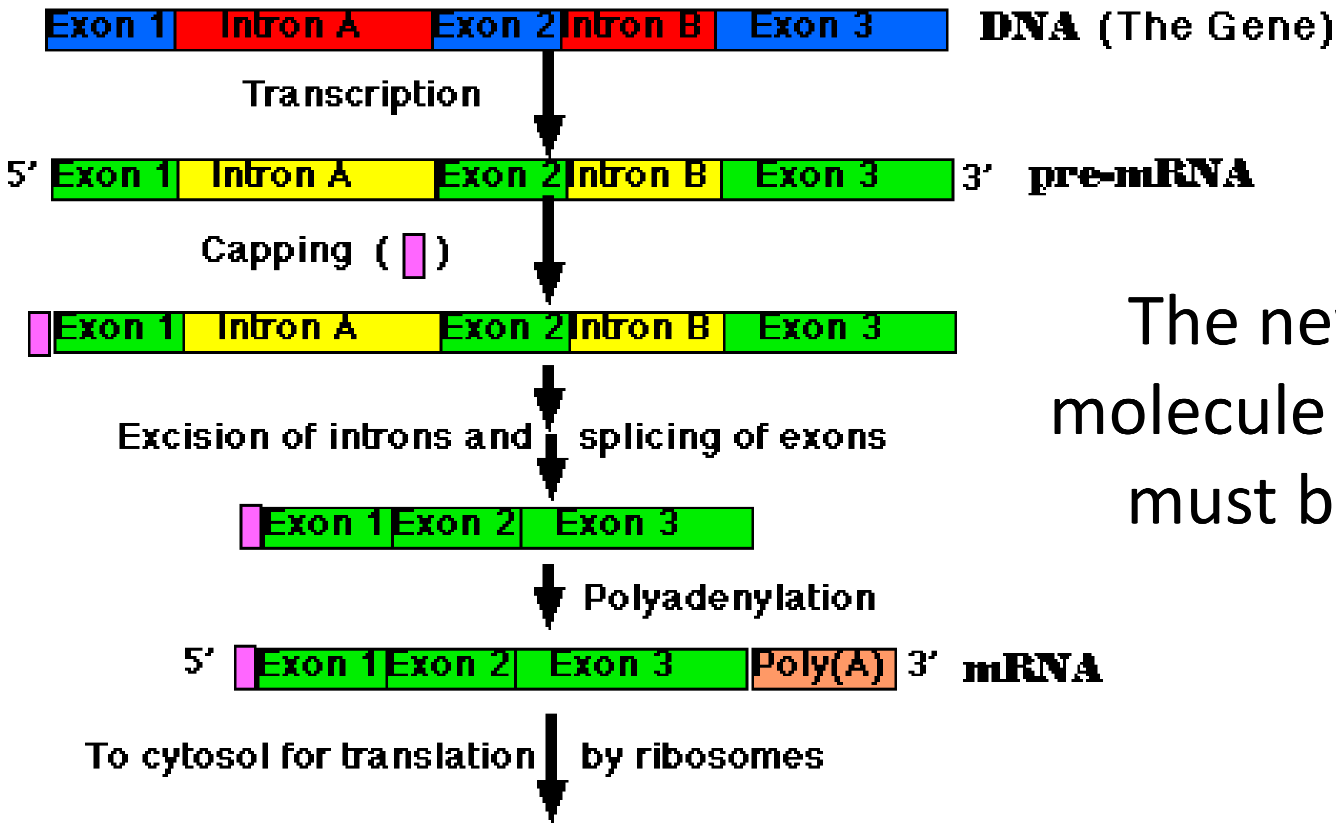
- **Exception**: T (in DNA) is replaced with U (in RNA).

Give the products when the following sequence of DNA is transcribed.

3'-A T C C G T…
5'-T A G G C A…

Processing RNA

In eukaryotic cells, transcription isn't just copying.



The newly made molecule (pre-mRNA) must be *capped*.

<u>introns</u>: unwanted, unneeded portions

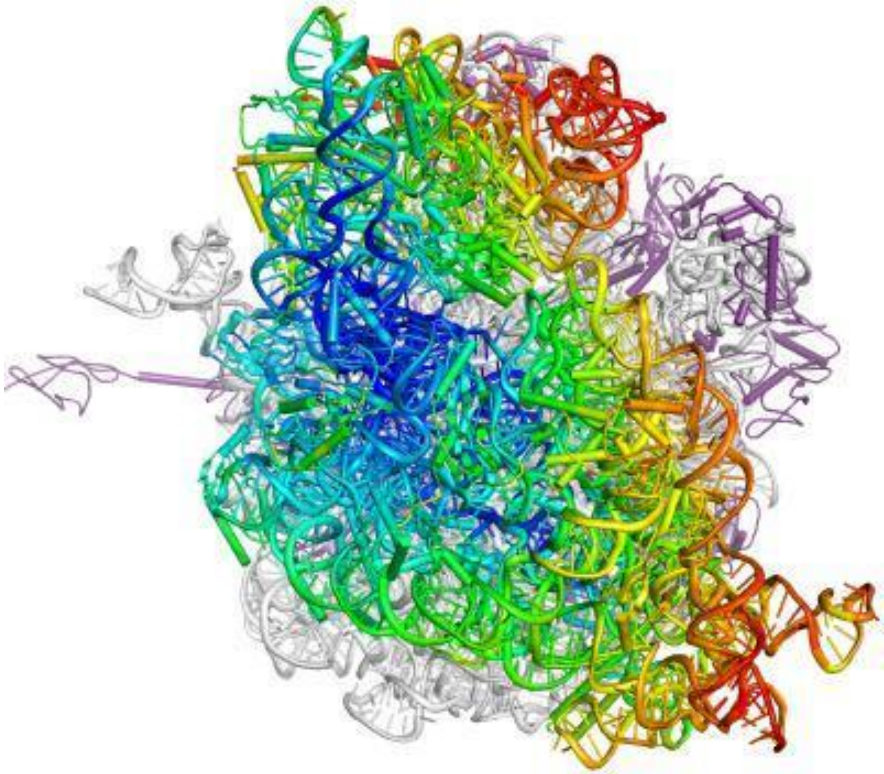
<u>exons:</u> portions that will be expressed as proteins

Practice Problem

Give the products after
replication/transcription for:

Replication:	Transcription:
5’-ACGTCCGGAA-3’	5’-CGTGTGGGGAATAA-3’
5’-GTTTAATCCG-3’	5’-TTGAGGGACCGA-3’
5’-AACGGGAACTAC-3’	5’-CCGAATAAGA-3’

Translation



DNA/RNA consist of nucleotides while proteins consist of amino acids; essentially, they speak two separate languages.

It requires three types of RNA to interpret:
mRNA: information carrier
tRNA: the amino acid mover
rRNA: the factory

Human Ribosome: Large complex of rRNA and proteins that hydrolyzes amino acids together to form their amide linkages.

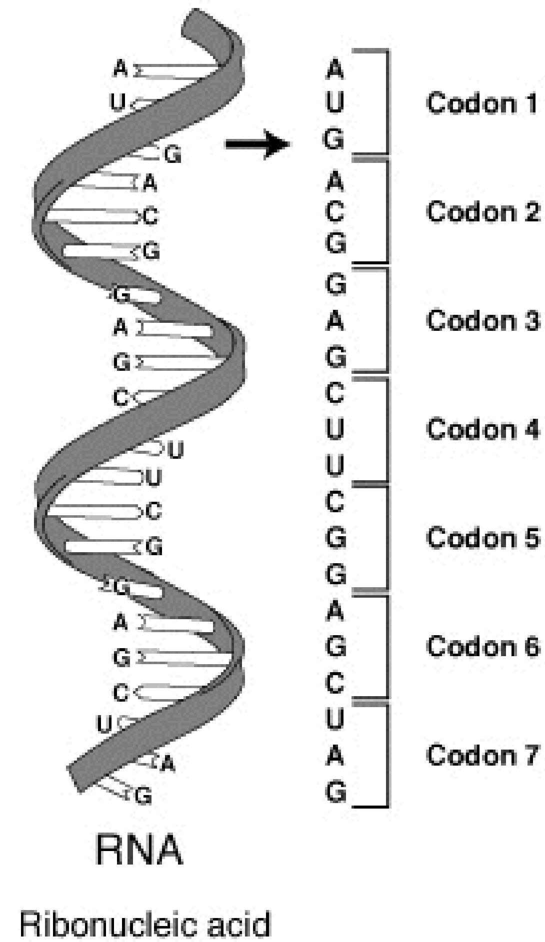
Codons

mRNA is always read from 5' to 3'. The produced proteins always start at the N-terminus and end at the C-terminus.

<u>codon</u>: three-base sequences that produce a single amino acid

<u>initiation sign:</u> the codon AUG signals translation to begin there

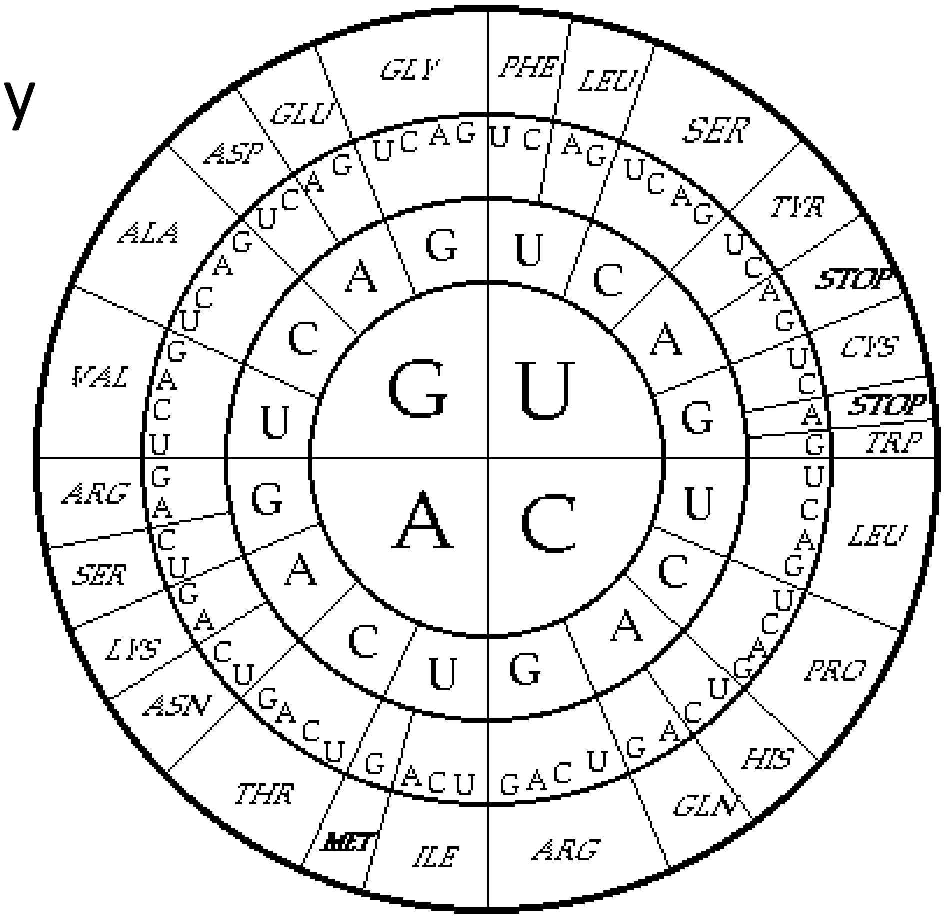
<u>termination sign</u>: the codons UGA or UAG or UAA signal the translation to end there



The Genetic Code

The *genetic code* interprets codons into amino acids.

The genetic code is virtually universal for every living organism.



RNA: AUG UAU CAC UGA

protein:

Practice Problem

Give the primary sequence of the protein that will be produced from the translation of the following mRNA strands.

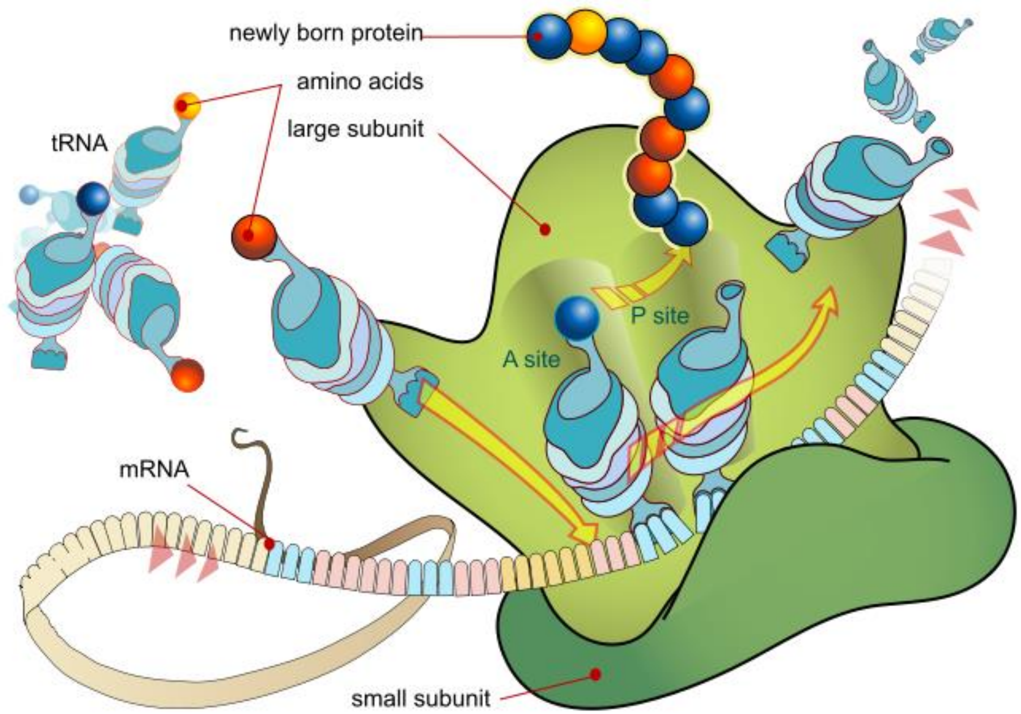
RNA: AUG UCC CCC ACG GCC UAG

RNA: UGU AUG GGC CAU GUU UGA GUC

Protein Synthesis

The synthesis of proteins has four major stages:

1. Activation: adds to ATP
2. Initiation: starts at *N*-formylmethionine (fMet)
3. Elongation: links amino acids in sequence
4. Termination: hydrolyzes and releases protein



Practice Problem

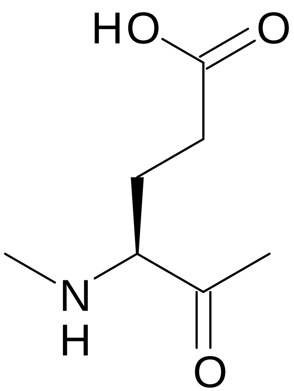
Design DNA strands that will code for the following peptides.

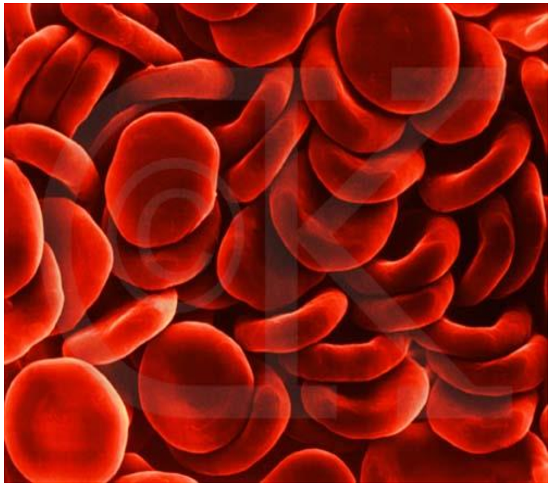
Met-Pro-His-Thr-Asp-Glu-Gly

Met-Thr-Val-Arg-Ser-Lys-Asn-Leu

Sickle Cell Anemia

Healthy Hemoglobin

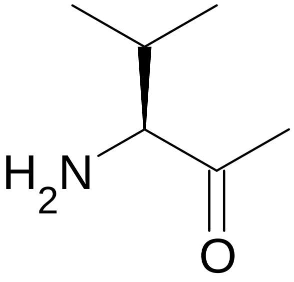


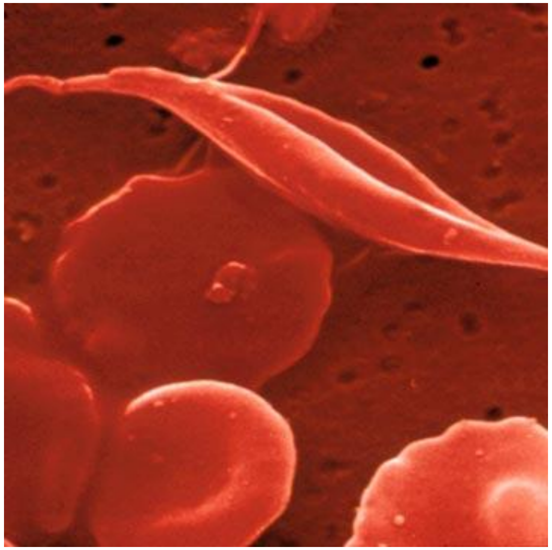


Glutamic acid is hydrophilic due to ionic charges.

Val-His-Leu-Thr-Pro-Glu-Glu-Lys-Ser-Ala...

Mutated Hemoglobin



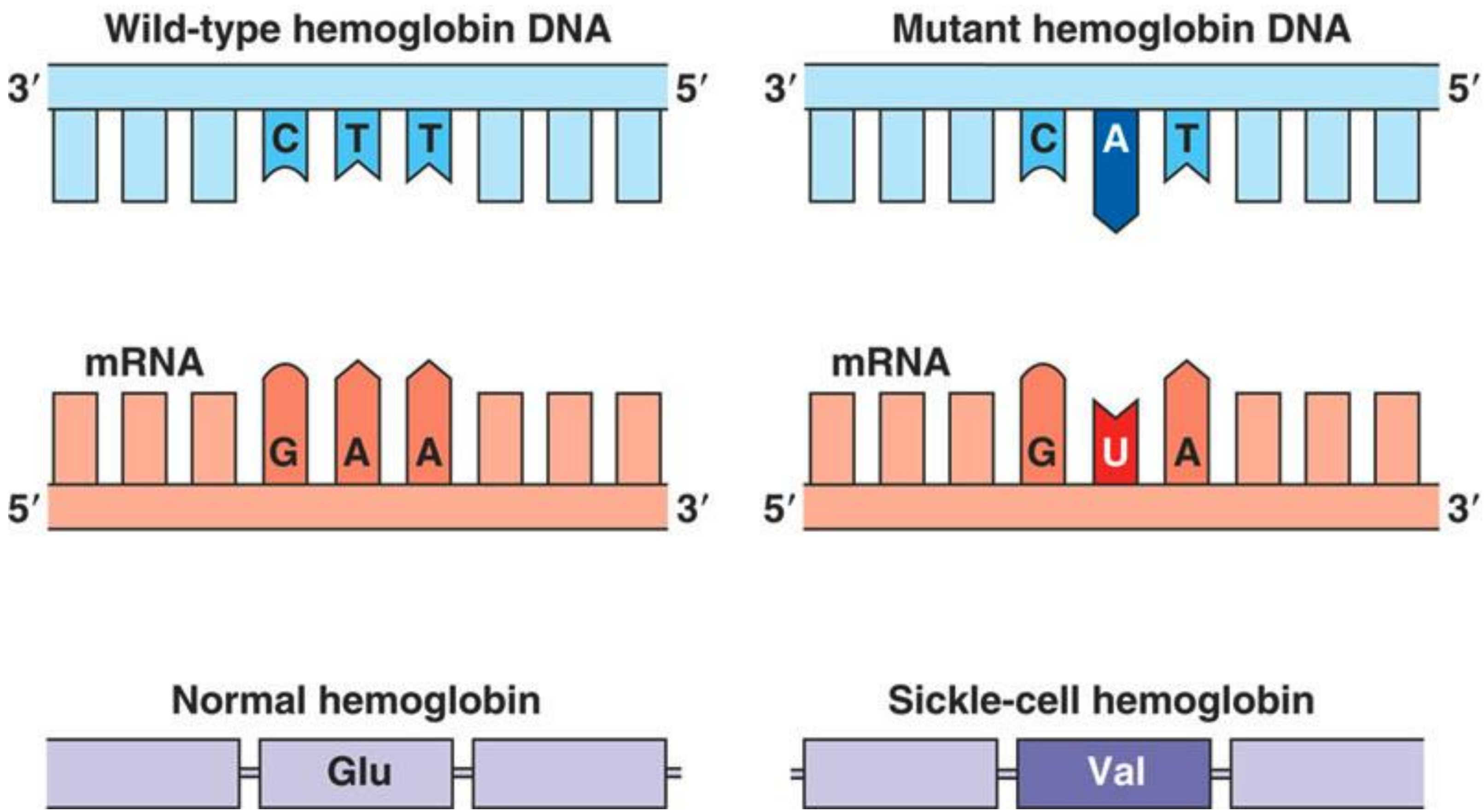


Valine is an aliphatic, nonpolar amino acid, making it hydrophobic.

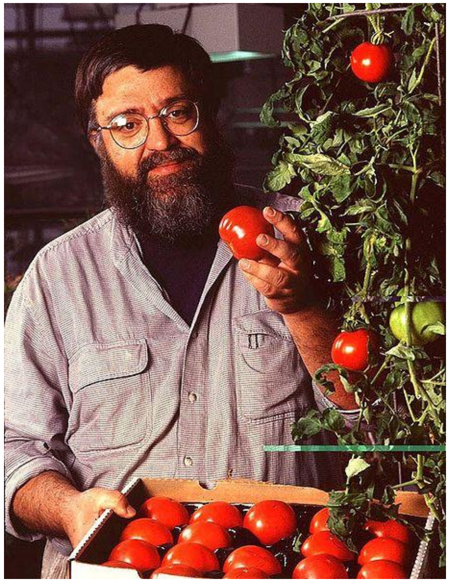
Val-His-Leu-Thr-Pro-Val-Glu-Lys-Ser-Ala...

DNA Mutation

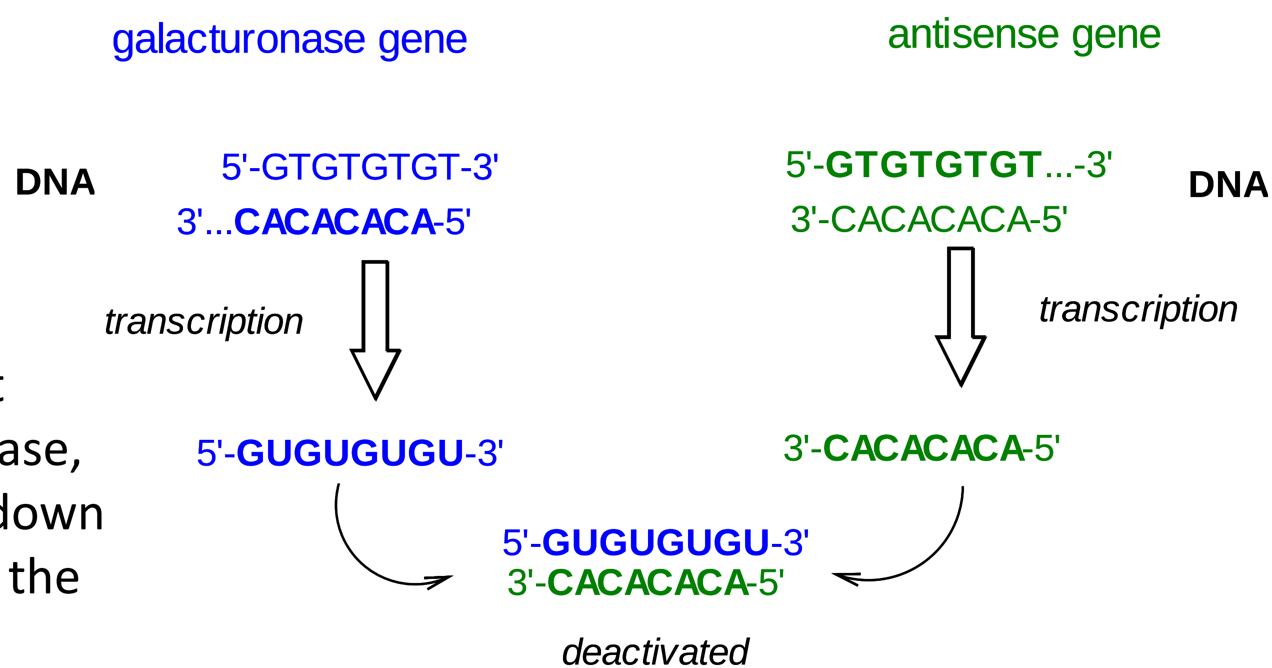
The mutation in the hemoglobin protein can be tracked back even further to a mutation in the DNA.



Genetic Modification



The Flavr Savr tomato was genetically engineered by RNAi (RNA interference) to prevent spoiling and degradation.

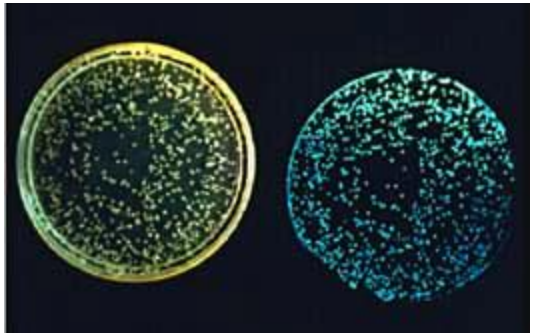


galacturonase: gene that produces polygalacturonase, the enzyme that breaks down the pectin in the walls of the fruit.

Quorum Sensing

<u>gene regulation:</u> turning genes “on” or “off” to control expression.

In bacteria, this is often accomplished through *quorum sensing,* or a coordinated, timed control of a behavior due to population density.



Bobtail Squid: Contains V. fischeri, a bioluminescent

Genetic Mutations

On average, one error for every 10 billion bases occurs.

mutations*:* miscopying of the DNA during replication, or a base error during transcription in protein synthesis.

DNA: …GTT…
replication → …ATT…
transcription → …UAA…
translation → STOP

RESULT: Protein produced is terminated too early.

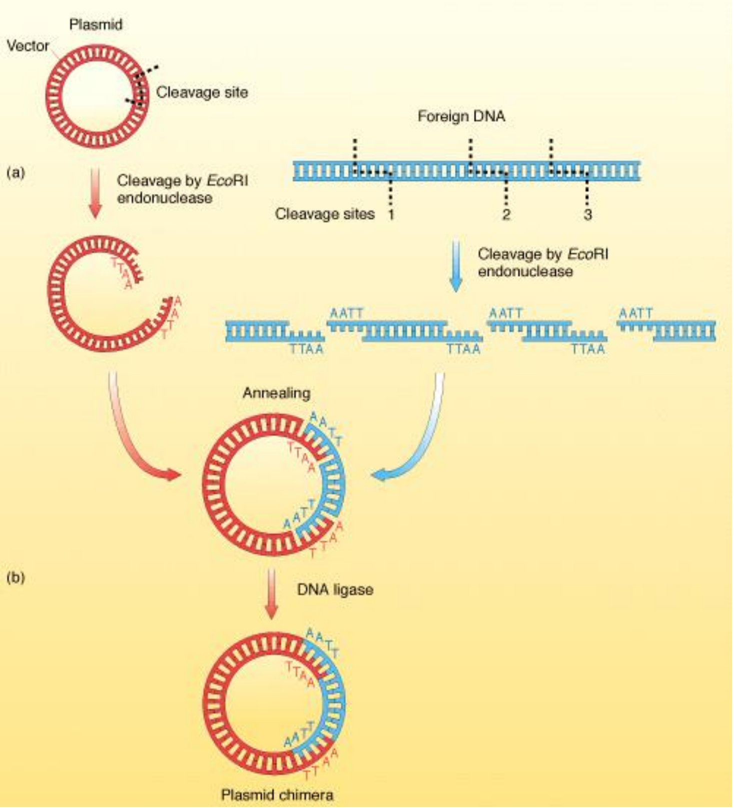
mutagens: organic compounds that react with the DNA to force mutations.

Recombinant DNA

recombinant DNA: splicing foreign DNA sequences into a cell to produce a desired effect.

Escherichia coli., a bacteria, contains plasmids.

“Humulin” was produced by inserting the gene for insulin production into *E.coli* and sold as an alternative to synthetic insulin.



Gene Therapy

Gene therapy is a huge area of research. If gene expression can be understood and controlled, then hereditary diseases can be snuffed out.

Recall that over 50% of the genes in the human body have no known function.