Name ____ Pd. _________

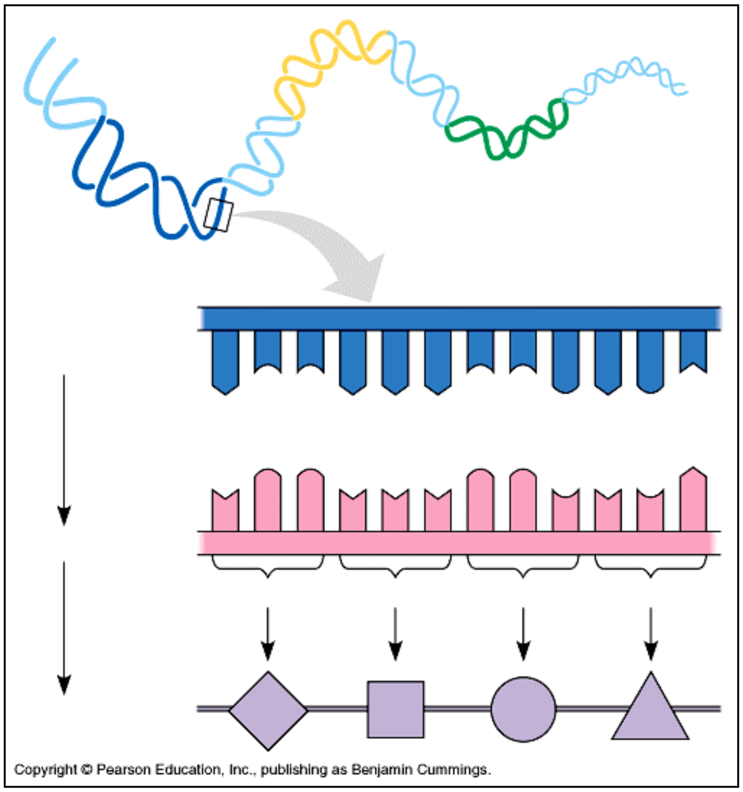
DNA → RNA → Protein: The Central Dogma

1. The Big Picture:

DNA copies itself (***REPLICATION***) usually so the cell can divide; DNA makes RNA (***TRANSCRIPTION***), RNA makes protein (***TRANSLATION***), and protein is what does just about everything important in our bodies. These are the "Big Three" processes in molecular genetics. Know them, live them.

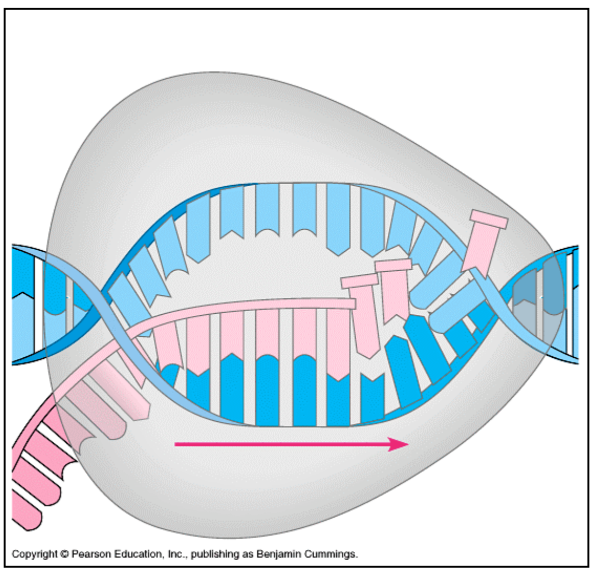
2. The Big Picture Diagram→

•Things to label:
- -Gene 1, gene 2 and gene 3 (the 3 dark portions on the double helix)
- -Transcription
- -Translation
- -DNA segment
- -mRNA segment
- -protein segment
- -one codon (any)
- -If the DNA sequence is ACCAAACCGAGT, label all the complementary mRNA bases and then use the translation chart on the front to determine which amino acids have been produced



3. Transcription ↓

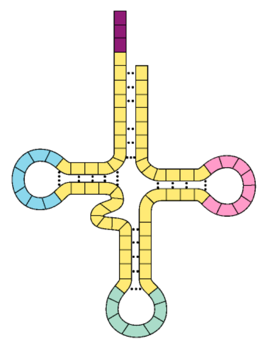
- -RNA Polymerase
- -mRNA strand
- -DNA



4. tRNA Molecule →

•Label the following items on this diagram of a tRNA molecule →

A-Attachment site for amino acid
B-Anticodon



5. One gene-one polypeptide Hypothesis

6. Translation dictionary →

This diagram shows which codons translate into which amino acids. Translate the following codons into amino acids:

AAU = ____________________

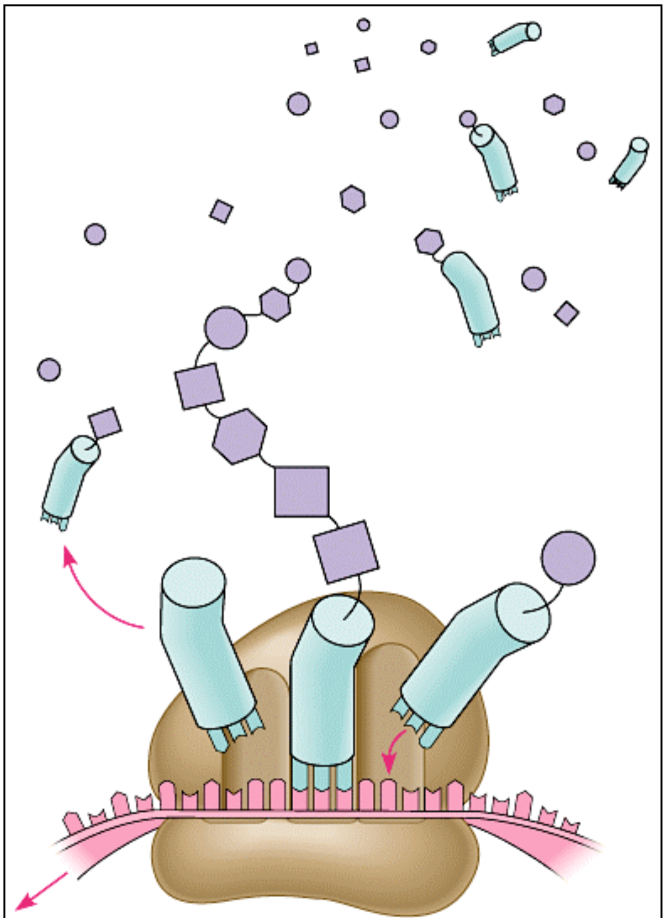
GAC = ____________________

UAA = ____________________

AUG = ____________________

Second base

First base (5′ end)	U	C	A	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



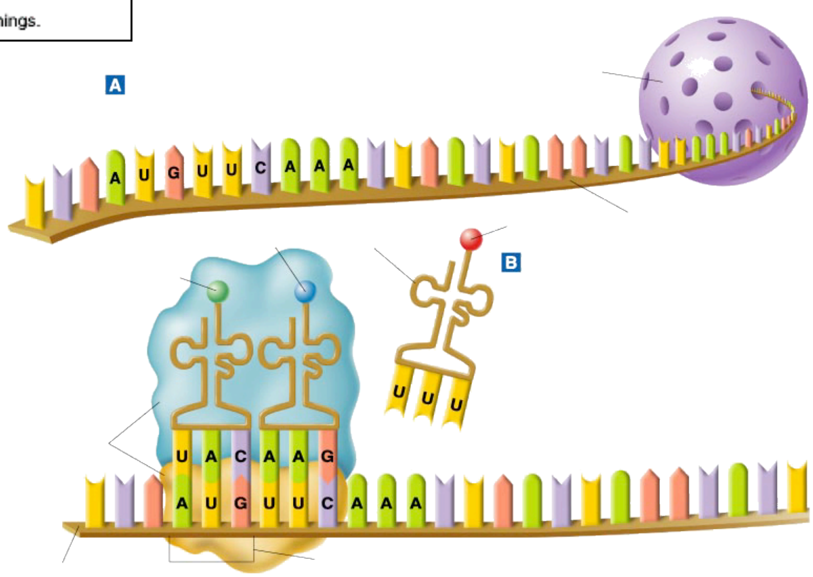
← 7. Translation Diagram

● Label the following items:
- A-a tRNA
- B-an amino acid
- C-mRNA
- D-ribosome
- E-an anticodon
- F-Choose appropriate nitrogen bases for the 6 bases on the codon and anticodon currently attached

8. Central Dogma Practice Labeling →

•Label the following items on this 2-step diagram:

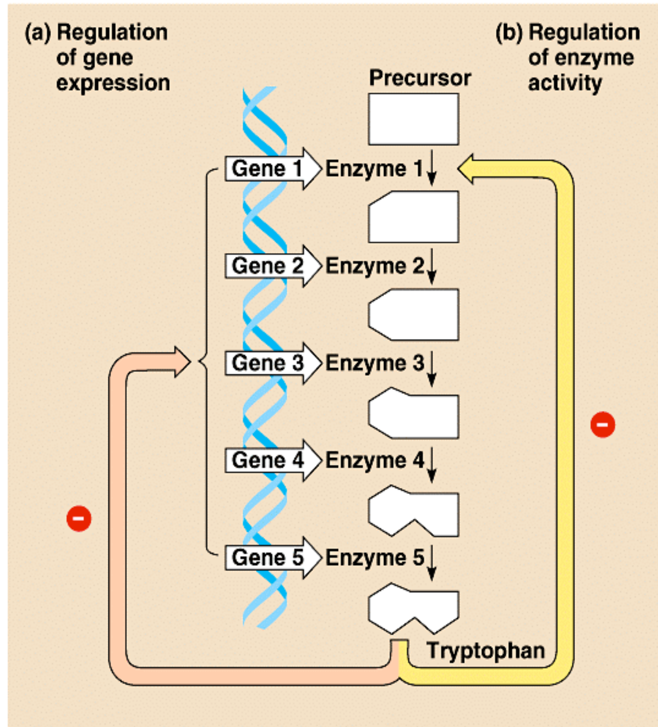
- A-nucleus
- B-mRNA leaving nucleus
- C-mRNA at ribosome
- D-tRNA (any one)
- E-amino acid (any one)
- F-ribosome
- G-a codon (any one)
- H-an anticodon (any one)
- J-nitrogen bases (any one)
- K-sugar/phosphate backbone



Gene Control & Expression

9. <u>Negative Feedback</u> (all cells)

a) Remember that when you need to convert one molecule into another, it is often a multi-step process. Each step requires a different enzyme, which means it requires a different gene to be transcribed into mRNA. This diagram shows the process of converting "pre-tryptophan" into tryptophan, an amino acid that you can manufacture. How many steps are required? ______ How many enzymes are required? _______.



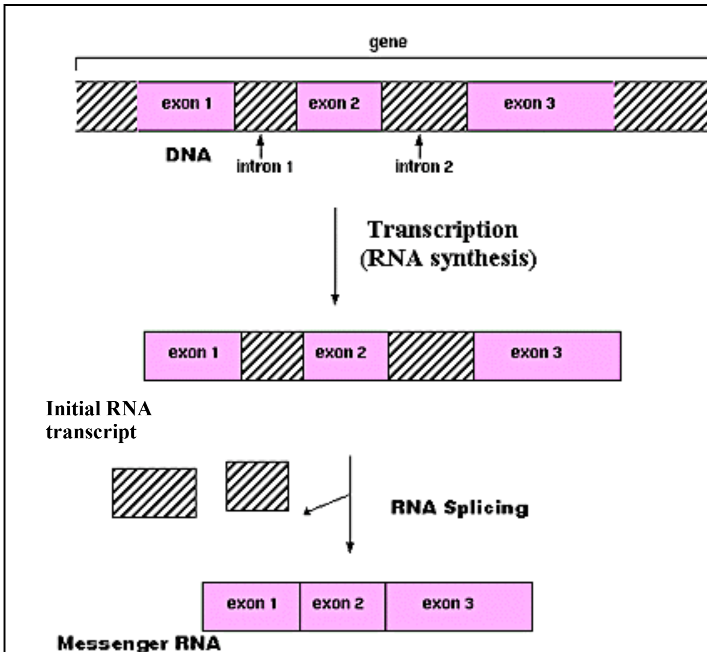
b) Remember also when we discussed Negative Feedback, in which the _________________ of a reaction actually turns _________ its own production. In this case, tryptophan turns off enzyme #________, which ultimately stops the production of any more tryptophan.

c) One thing we haven't discussed is how a molecule can not only deactivate an enzyme, but it can also stop a gene from being transcribed! In this diagram, note that it is turning its own production off by deactivating both enzyme #______ <u>and</u> gene #_______.

d) Make sure you understand the diagram before continuing.

<u>10. RNA Splicing/Processing (Eukaryotes)</u>

a) We have learned that mRNA is transcribed from __________ in the cell's __________________________. Before go to a ribosome in the cytoplasm, though, it must be processed first. The most important step in this is the removal of certain parts of the mRNA molecule. These parts that are removed are called **<u>INTRONS</u>**, and they stay in the nucleus, are digested into nucleotides and are reused the next time we need to make some RNA. They do not code for proteins. The remaining portions of the mRNA (the **<u>EXONS</u>**, which are quite <u>ex</u>cellent as they <u>ex</u>it the nucleus) are glued back together to be used for protein synthesis.



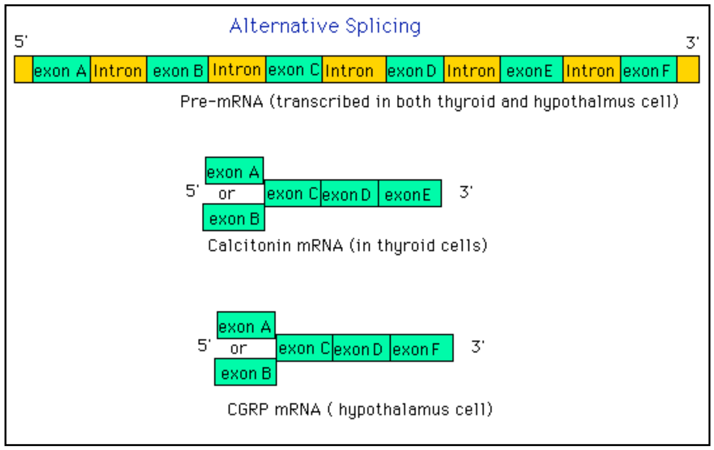
RNA synthesis and processing

b) This could never occur in bacteria because:

c) Consider the following sequence of letters: **CTHERAOPSLOORFIZDAMSTOY**

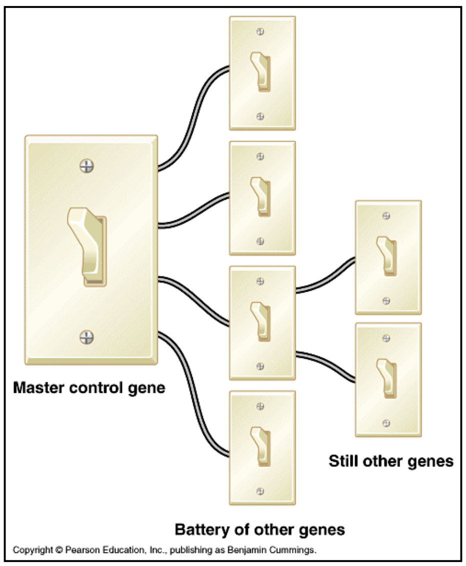
d) If you could cross out some of the letters, but not others, to create as many words as possible, how many could you make? List some of them here:

e) Your DNA works the same way. Using the same piece of newly-minted RNA, you can cut & paste it differently in order make different versions of the mRNA that leaves the nucleus. In this way, the same piece of DNA can be used to create several different pieces of functional mRNA. This is called **<u>ALTERNATIVE RNA SPLICING</u>** (see image →). It's like going to IKEA, where you can mix and match several basic furniture parts to make lots of different pieces.



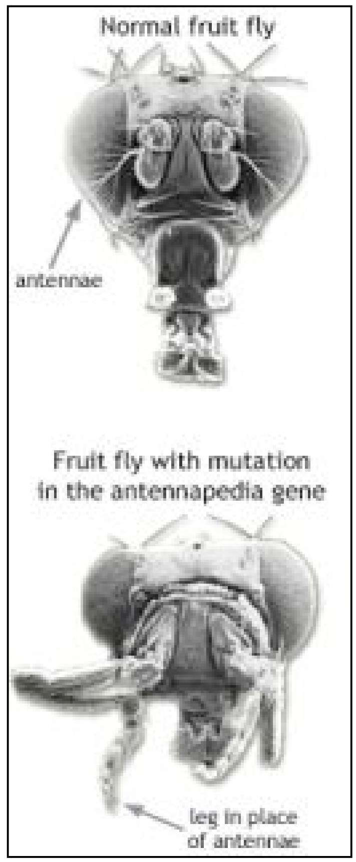
f) Hmm…this new discovery calls into question what other hypothesis that we just learned about?

11. <u>Homeotic Genes</u> (animals)



a) These master control genes are VERY important. They direct the embryonic development of animals' major body parts by controlling lots of other genes. Even a small mutation in one of these produces huge effects in the organism.

b) Mutations cause parts of the animal to arise in the wrong place, e.g. unfortunate fruit fly→



12. <u>Differentiation</u> (most multicellular organisms)

a) During development, differentation is the process by which cells become specialized in structure and function. Cell division alone would produce only a great ball of identical cells, which would be no fun at all. These different kinds of cells are then organized into tissues and organs. Differentiation is when cells choose a career path: liver, bone, kidney, skin, etc.

b) But if all cells have the same DNA—the same instructions—then how can they perform completely different jobs? Because they express different genes.

c) Give two examples of a protein that ALL human cells would need to express:

d) Give two examples of proteins that only very specific sorts of human cells would need to express (and name the sort of cell that would express them)

e) In an adult human, very little differentiation is still happening. Where could you find these last vestiges of this embryonic process occurring?

f) Cells that have not differentiated are called **STEM CELLS**.

g) The big question for future research is, after a cell has turned off enough genes to undergo differentiation, can we find a way to turn them back on? If we can do this, we can make a plain old cheek cell into a brain cell or a bone cell or anything else!

h) One method of differentiation is a bit extreme. In some cases, normal development requires the ultimate sacrifice: cell suicide. (Actually, it's called **APOPTOSIS**, or programmed cell death.)

e.g. This occurs during the normal development of the human hand. Your hands begin not with separate fingers, but with webbed fingers. Then the cells in between the fingers die, leaving 5 separate piggies.

13. Genes and cancer

a) **PROTO-ONCOGENES** (literally, "early cancer gene") are genes that produce proteins that stimulate normal cell growth and division, and so they have *essential* functions in *normal* cells. But what happens when you mess up a cell's ability to control its cell growth and division? Yes. Then we call then **ONCOGENES**.

b) The big question is, how do the proto-oncogenes become oncogenes? An oncogene occurs when a mutation produces an increase in the production or activity level of the proto-oncogene's protein.

e.g. 1--Movements of DNA within the genome: Malignant cells frequently have chromosomes that have been broken and rejoined incorrectly, e.g. a gene that should only be activated occasionally moving next to an extremely active promotor.

e.g. 2--Multiple copies of proto-oncogenes by transposons, which would of course increase the number of gene copies and therefore their activity level.

Bacterial gene expression and operons

14. What is an operon?

If it requires 5 enzymes to convert one molecule into another, and the absence of any one of them prevents the production of whatever molecule you're trying to make, then there must be a way to ensure that when they are needed, they all show up. A Bacteria cell's simple solution to this problem is called an **OPERON**. An operon is simply a cluster of functionally related enzyme genes that is transcribed as a unit. This way, when you transcribe one of them, you transcribe them all. Makes sense, eh?

15. Parts of an operon

- An operon consists of 3 parts:

a) the actual genes that code for the enzymes

b) a **PROMOTOR** region, where RNA polymerase first attaches, sort of like "Go" in Monopoly.

c) an **OPERATOR** region, located between the promotor and the gene, that acts as an on/off switch if a repressor protein binds to it and blocks part of the promotor.

d) There is a 4th part that is involved, but it is not part of the operon. A **REGULATOR GENE** makes a protein called a repressor protein, which can be used to block transcription of the operon.

16. How does an operon work? A closer look at the LAC OPERON

a) It is named for **LACTOSE** (milk sugar--$C_{12}H_{22}O_{11}$), because its genes code for enzymes that metabolize lactose.

b) The operon can either be ON or it can be OFF.

c) If nothing is blocking the promotor, then RNA polymerase can bind to the promotor and thus transcribe the genes. (ON)

d) However, if a **REPRESSOR** protein (a product of a regulatory gene) attaches to the operator, it blocks transcription of the operon's genes by physically blocking the RNA polymerase from attaching to the DNA to transcribe it. (OFF)

e) So what determines whether the repressor protein is repressing or not? It turns out that the repressor protein is like an enzyme with an allosteric site. It can use its active site to attach to the operator and therefore block RNA polymerase UNLESS something attaches to its allosteric site and changes its shape. And what sort of thing can do this? Lactose! If lactose is there, then it attaches to the repressor protein, prevents it from blocking RNA polymerase, and the operon is successfully transcribed. This means the cell will create all those wonderful lactose-digesting enzymes and get ride of all that lactose. This happens when it is given milk as food.

f) But what happens when the lactose is gone? There is nothing left to attach to the repressor, which is free to bind to the operator, and prevent the RNA polymerase from attaching, which ultimately stops production of the lactose-digesting enzymes. Why stop? Making proteins uses energy, and making useless proteins wastes energy.

g) And of course this continues until lactose appears again.