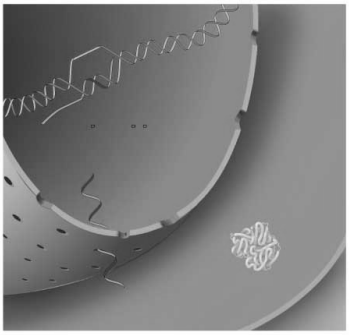
Chapter 10: Central Dogma
Gene Expression and Regulation



Fact 1:
DNA contains information but is unable to carry out actions

Fact 2:
Proteins are the "workhorses" but contain no information

THUS
Information in DNA must be linked with proteins

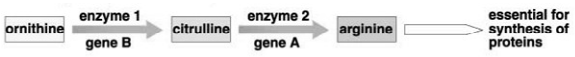
HOW?

$$\text{Substrate 1} \xrightarrow[\text{Gene A}]{\text{Enzyme A}} \text{Substrate 2} \xrightarrow[\text{Gene B}]{\text{Enzyme B}} \text{Substrate 3}$$

Beadle & Tatum: Bread mold experiments (1940s)

Beadle & Tatum: Neurospora molds

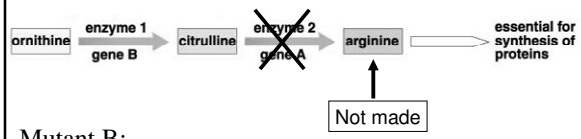
- Examined different Neurospora mutants
  - ❖Neurospora = bread mold organisms.
- Neurospora has the following metabolic pathway:



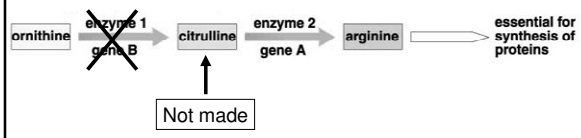
- Neurospora mutants
  - ❖Mutant A could not produce enzyme 2
  - ❖Mutant B could not produce enzyme 1

Neurospora mutants

Mutant A:



Mutant B:



- Generally, one gene codes for one protein (polypeptide)

How Does Information Travel from DNA to Ribosomes?

Answer: RNA (Ribonucleic Acid)

- RNA works as intermediary between DNA and ribosomes
- RNA structure differs from DNA structure in 3 respects:
  1) RNA is single-stranded
  2) RNA has ribose sugar in backbone (DNA = deoxyribose)
  3) RNA has base uracil instead of thymine (A $\rightarrow$ U)

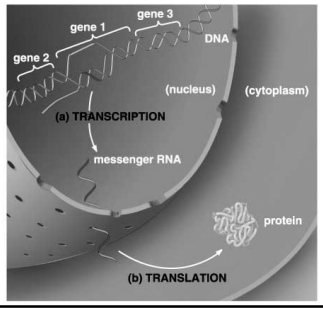
See Table 10.1 on page 169 for Comparison

- **DNA codes for synthesis of 3 RNA types:**

1) Messenger RNA (mRNA)
   - Carries code from DNA to ribosomes
2) Ribosomal RNA (rRNA)
   - Combines with protein to form ribosomes
3) Transfer RNA (tRNA)
   - Carries amino acids to ribosomes

Central Dogma of Biology:

DNA $\xrightarrow[\text{Nucleus}]{\text{Transcription}}$ RNA $\xrightarrow[\text{Cytoplasm}]{\text{Translation}}$ Protein



The genetic code : the language of life

- 4 bases
  - ❖adenine, thymine, cytosine, guanine
- 20 amino acids
- 4 bases, doublets only has 16 combinations
- So it must be a ***triplet*** code
  - ❖Codons are triplets of nucleotides.

Breaking the code

- Researchers at National Institute of Health (NIH) made artificial message
  - ❖RNA 1: UUUUUUUUU
  - ❖Protein 1: Phe-phe-phe
  - ❖RNA 2: AAAAAAAAA
  - ❖Protein 2: Lys-lys-lys

The Genetic Code: The "Language" of Life

The genetic code is a triplet code:

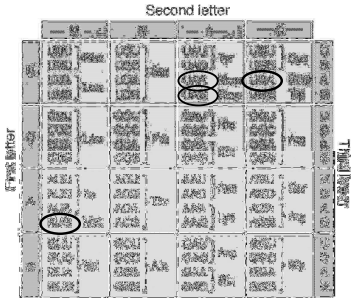
- Three bases (condon) code for 1 amino acid
- More than 1 codon for each amino acid (Table 10.3)

START	Alanine	Lysine	Arginine	Alanine	STOP
A U G	G C G	A A G	A G G	G C A	U A G

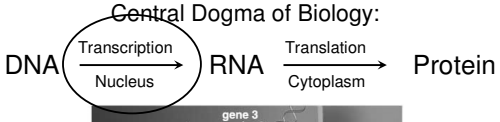
- Punctuation codons (start / stop) exist in genetic code
  - Start = AUG
  - Stop = UAG, UAA, UGA

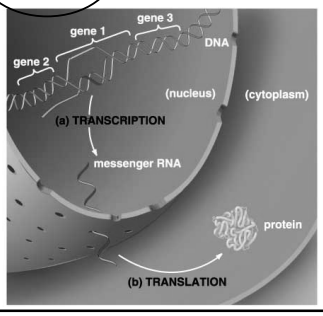
The genetic code

- Will be provided on the final, but you must know how to read it.

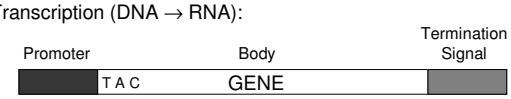


Central Dogma of Biology:





Transcription (DNA → RNA):

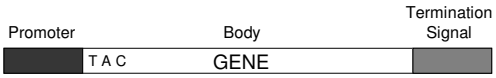


Transcription produces a *single strand* of RNA that is complementary to one strand of DNA

Step 1: Initiation

- **RNA Polymerase** binds to promoter region
  - Promoter = Non-coding region of gene
  - Different version of RNA polymerase synthesizes each type of RNA (mRNA, rRNA, & tRNA)

Transcription (DNA → RNA):

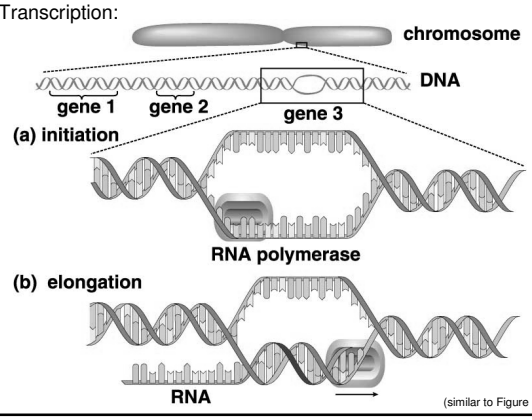


Step 2: **Elongation**

- RNA Polymerase "forces" DNA to partially unwind
  - RNA Polymerase synthesizes complementary copy
  - Template Strand = DNA strand being transcribed
- Base pair rules apply except uracil replaces thymine:
  - Guanine → Cytosine
  - Adenine → Uracil

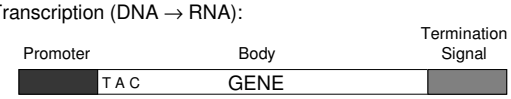
A	T	C	G	A	A	A	T	C	G	C	G	A	G	DNA
U	A	G	C	U	U	U	A	G	C	G	C	U	C	RNA

Transcription:



(similar to Figure 10.4)

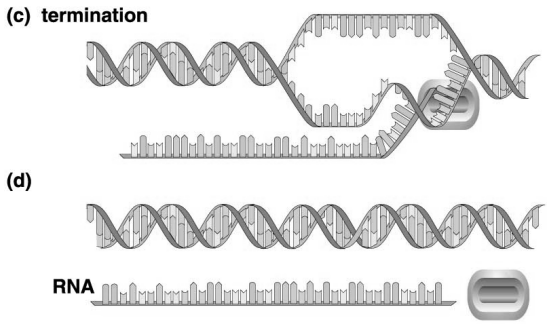
Transcription (DNA → RNA):



Step 3: Termination

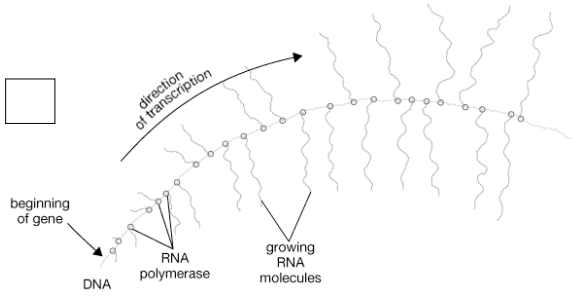
- RNA polymerase reaches termination signal
  - ❖ RNA polymerase detaches from DNA strand
  - ❖ RNA molecule detaches from RNA polymerase
  - ❖ DNA zips back up

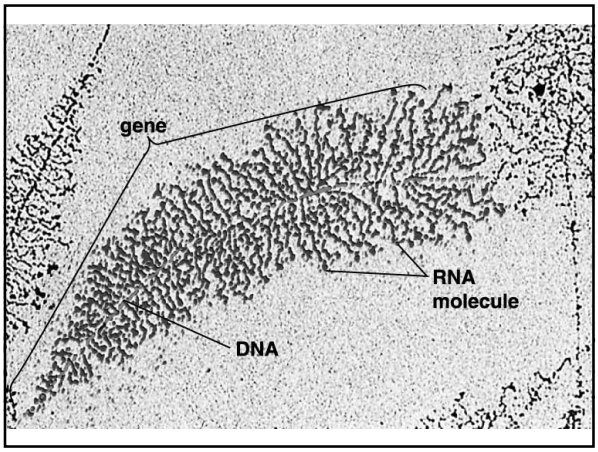
Transcription:



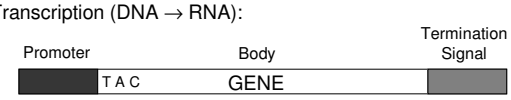
(similar to Figure 10.4)

Multiple RNA polymerase can transcribe a single gene at the same time





Transcription (DNA → RNA):



Step 3: Termination

- RNA polymerase reaches termination signal (stop codon)
  - RNA molecule detaches from RNA polymerase
  - RNA polymerase detaches from DNA strand
  - DNA zips back up

The transcription of genes into RNA is selective:

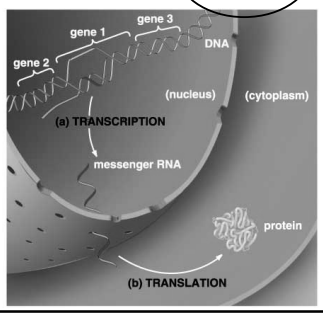
1) Only certain cells transcribe certain genes
   - Insulin (hormone) → Pancreas
2) Only one strand of DNA (template strand) is copied

Let's see that in action!

- transcription

Central Dogma of ~~Biology~~:

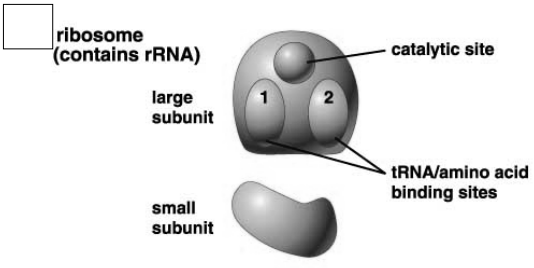
DNA —Transcription (Nucleus)→ RNA —Translation (Cytoplasm)→ Protein



Translation (RNA → Protein):

1) mRNA carries code for protein from nucleus to cytoplasm
   - Exits nucleus via nuclear pores
2) mRNA binds to ribosomes (protein factories) in cytoplasm
   - Ribosomes = rRNA & proteins
   - Composed of two (2) sub-units:
     1) Small Ribosomal Sub-unit
        - Binds mRNA and part of tRNA
     2) Large Ribosomal Sub-unit
        - Binds other part of tRNA and has enzymatic site where amino acids are linked together

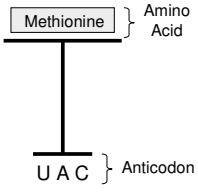
Ribosomes:



(Figure 10.2)

Translation (RNA → Protein):

1) mRNA carries code for protein from nucleus to cytoplasm
2) Ribosomes (protein factories) bind to mRNA in cytoplasm
3) tRNA delivers appropriate amino acid to ribosome
   - tRNA has 3 exposed bases that form base pairs with the mRNA codon (Anticodon)
   - tRNA has correct amino acid attached for *mRNA codon*
     - 61 unique tRNAs

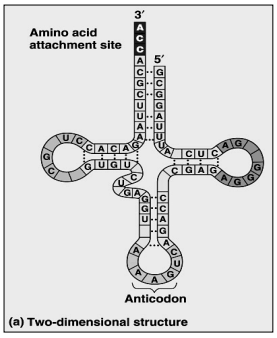


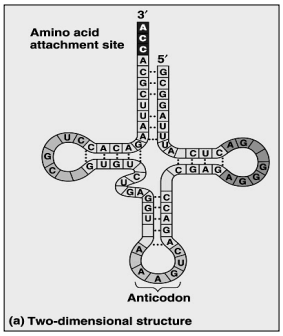
3. Transfer RNAs (tRNAs)

- Many different kinds
- Anticodon

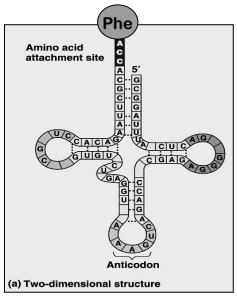
  = 3 rNTs

  base-pairs with mRNA codon during translation.





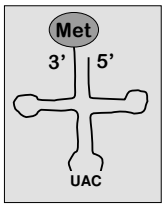
tRNA anticodon:	**3' A A G 5'**
mRNA codon:	**5' U U C 3'**



Which aa would this tRNA carry? **Phe**

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

If tRNA anticodon = 3′ UAC 5′
amino acid = **Met**



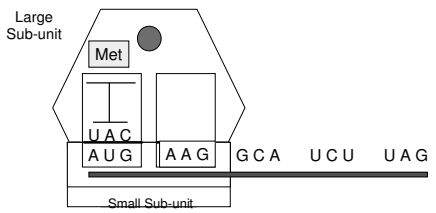
Initiator tRNA basepairs with start codon

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

Translation Steps (RNA → Protein):

Step 1: Initiation

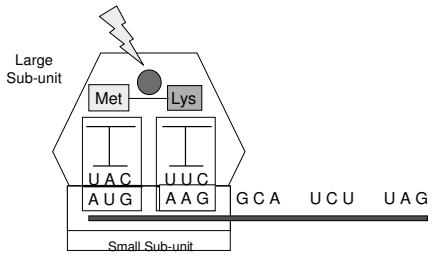
- mRNA binds with small subunit of ribosome
- tRNA with anticodon for start codon binds to mRNA
- Large sub-unit of ribosome binds to small sub-unit



Translation Steps (RNA → Protein):

Step 2: Elongation

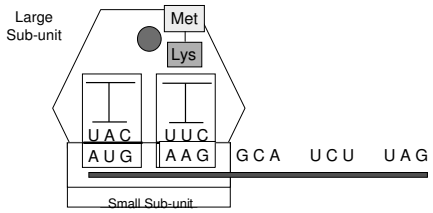
- The next tRNA with proper anticodon binds to mRNA
- Catalytic site joins amino acids together (**peptide bond**)



Translation Steps (RNA → Protein):

Step 2: Elongation

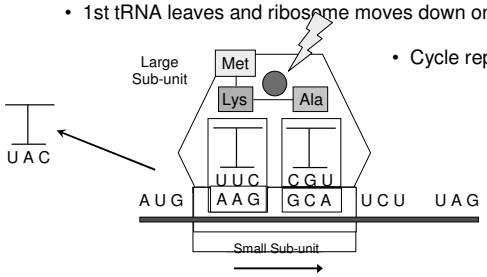
- The next tRNA with proper anticodon binds to mRNA
- Catalytic site joins amino acids together (peptide bond)
- 1st tRNA leaves and ribosome moves down one spot



Translation Steps (RNA → Protein):

Step 2: Elongation

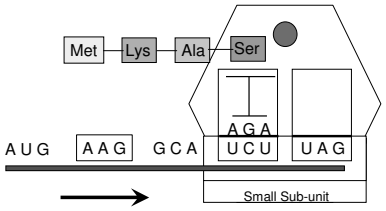
- The next tRNA with proper anticodon binds to mRNA
- Catalytic site joins amino acids together (peptide bond)
- 1st tRNA leaves and ribosome moves down one spot
- Cycle repeated



Translation Steps (RNA → Protein):

Step 3: Termination

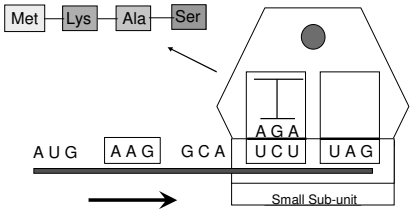
- Process continues until stop codon is reached
- Finished protein is released from ribosome



Translation Steps (RNA → Protein):

Step 3: Termination

- Process continues until stop codon is reached
- Finished protein is released from ribosome
- Sub-units of ribosome separate from mRNA



Translation Steps (RNA → Protein):

Step 3: Termination

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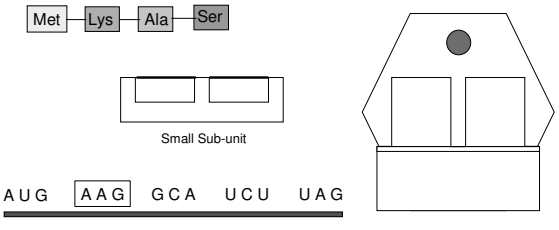
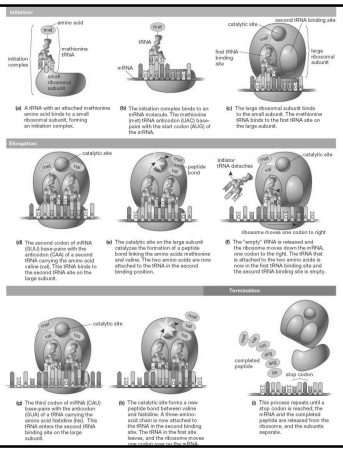


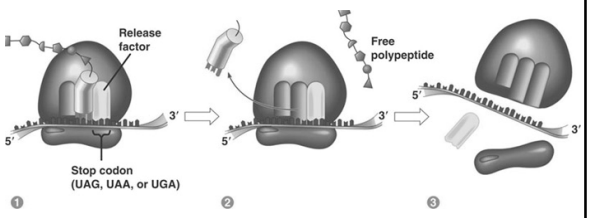
Translation:



(Figure 10.6)

When a stop codon is reached…

- Amino acid chain (polypeptide) is released.
- Ribosome separates into separate subunits.



Let's see translation in action!

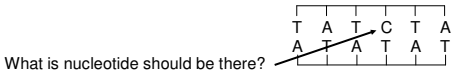
- Translation

Once Again - Mistakes Happen...

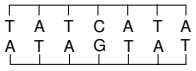
Mutation: Changes in the sequence of bases in DNA

Types of Mutations:

1) Point Mutation: A pair of bases is incorrectly matched



2) Insertion Mutation: One or more nucleotide pairs are inserted into a gene

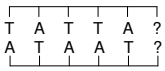


Once Again - Mistakes Happen...

Mutation: Changes in the sequence of bases in DNA

Types of Mutations:

3) Deletion Mutation: One or more nucleotide pairs are deleted from a gene

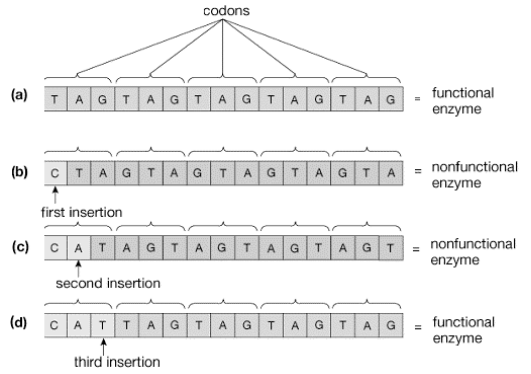


Possible outcomes of a point mutation (active gene):

1) Protein is unchanged (codes for same amino acid)
   - CTC and CTT still code for Leucine...
2) New protein equivalent to old protein
   - Replace hydrophobic AA with hydrophobic AA
   - Neutral mutations
3) Protein structure is changed (*e.g.* sickle cell anemia)
   - Usually cause problems
4) Protein function destroyed due to stop codon insertion
   - AAG codes for amino acid; ATG is stop codon

See Table 10.4...

What About Insertions and Deletions?



Insertions and deletions cause frameshift mutations

- Insertions and deletions, if they are not in multiples of 3, cause frameshift mutations.
  - ❖These mutations are often cause VERY severe problems.

correct reading frame:

THE FAT CAT ATE THE RAT

insertion:

THE NFA TCA TAT ETH ERA T

- If the insertion or deletion are in multiples of 3, they will still change the polypeptide because there is an extra amino acid in the chain.

Mutations provide the raw material for evolution...

A single mutation causes rabbits to be white instead of brownish gray

Eat me!

Try and find me!
I dare you.

Gene Regulation:

- Proper regulation of gene expression critical…
- 30,000 genes in human genome
  - ❖ Individual cells express small fraction of genes
  - ❖ Gene expression changes over time
  - ❖ Some genes never expressed

Regulation of genes can occur across Central Dogma:

1) Rate of transcription controlled:
   A) Regulatory proteins
      - Assist/block binding of RNA polymerase
   B) Chromosome condensation (tightly packed areas)
      - RNA polymerase can't access regions
   C) Chromosome inactivity (XX vs. XY chromosomes)

Barr Body: Inactive X chromosome in females

- Random during development for which X chromosome inactivates

All female vertebrates, including human females, are mosaics.

Gene Regulation:

- Proper regulation of gene expression critical…
- 30,000 genes in human genome
  - Individual cells express small fraction of genes
  - Gene expression changes over time
  - Some genes never expressed

Regulation of genes can occur across Central Dogma:

1) Rate of transcription controlled:
2) Translation occurs at different rates
   - Depends on stability of mRNA
3) Protein requires activation modifications
4) Life span of a protein controlled

Why are genes regulated?

- **Some proteins are only needed for certain activities**
  - ❖can cause problems when they are always produced.
- **Insulin**
  - ❖Needed to process glucose.
  - ❖Too much insulin = hypoglycemia which leads to death.