Lecture 24:

Regulation of gene expression

I. Generalities

Course 371

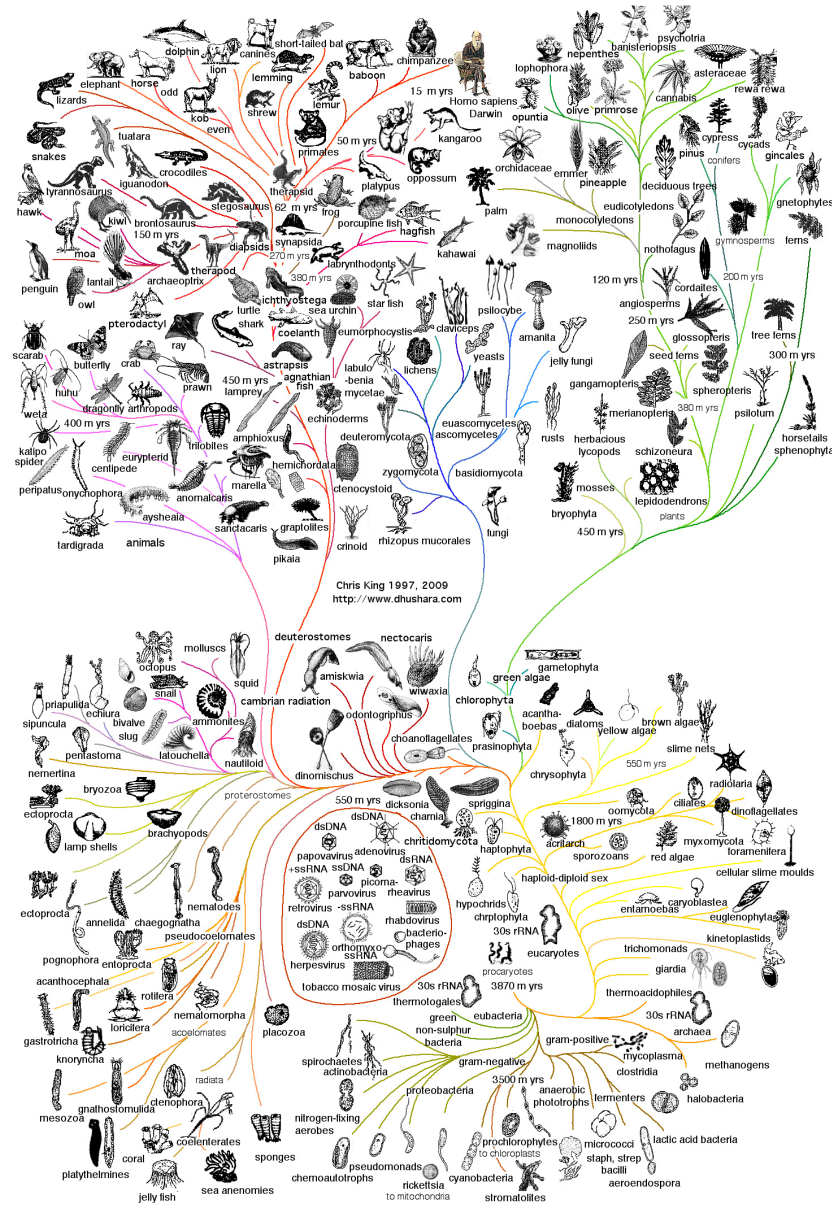
Lessons for life

AIMS

- Understand the the importance of the regulation of gene expression.
- Understand when gene expression can be controlled both in prokaryotes and eukaryotes.
- Understand the overall structure of the genes' molecular switches.
- Understand what DNA motifs are.
- Understand the different classes of regulatory proteins.

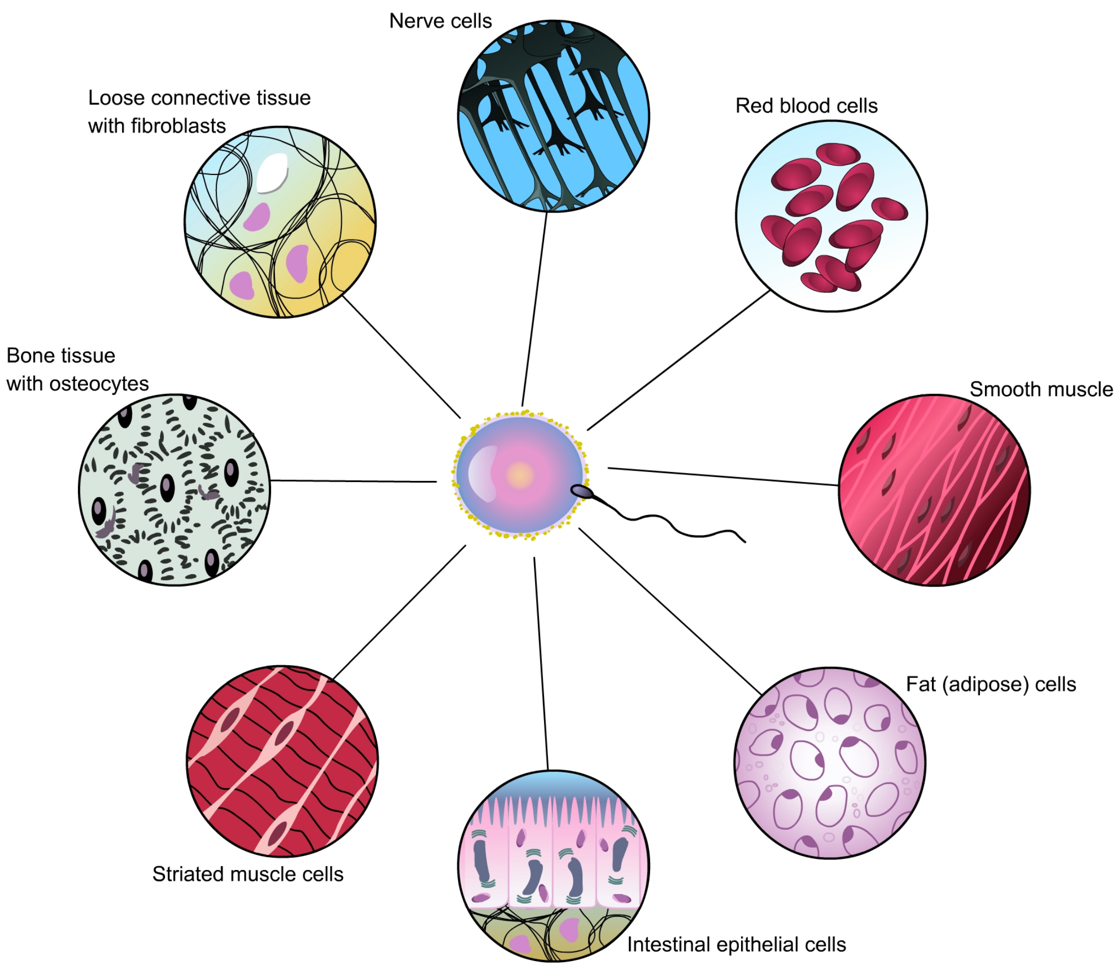
Overview

- DNA encodes all RNAs and proteins needed for the cell/ organism.
- Genes make almost! every character of a cell/organism.



Overview

One cell (zygote) divides and differentiates to make so many cell types



Overview

The differentiation depends on changes in gene expression

NOT

on a change in the genes or the nucleotides of the genome.

Overview

How do we know that the genes are the same in all cells and some have not been lost by some cellular mechanisms?

- Experiments that show that the genome of differentiated cells is the same and can be re-programmed to make any other cell type.
- Among such experiments are the cloning experiments.

Experiments: empty cell to synthetic bacteria

Chemical synthesis of a bacterial genome and placing it in an empty cell

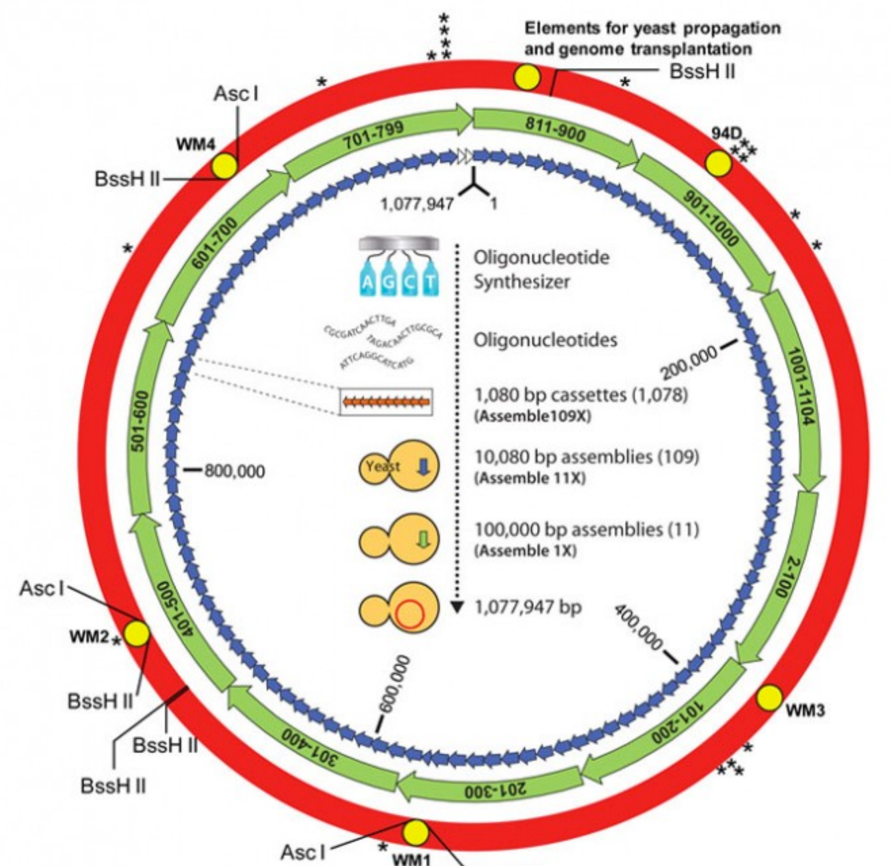
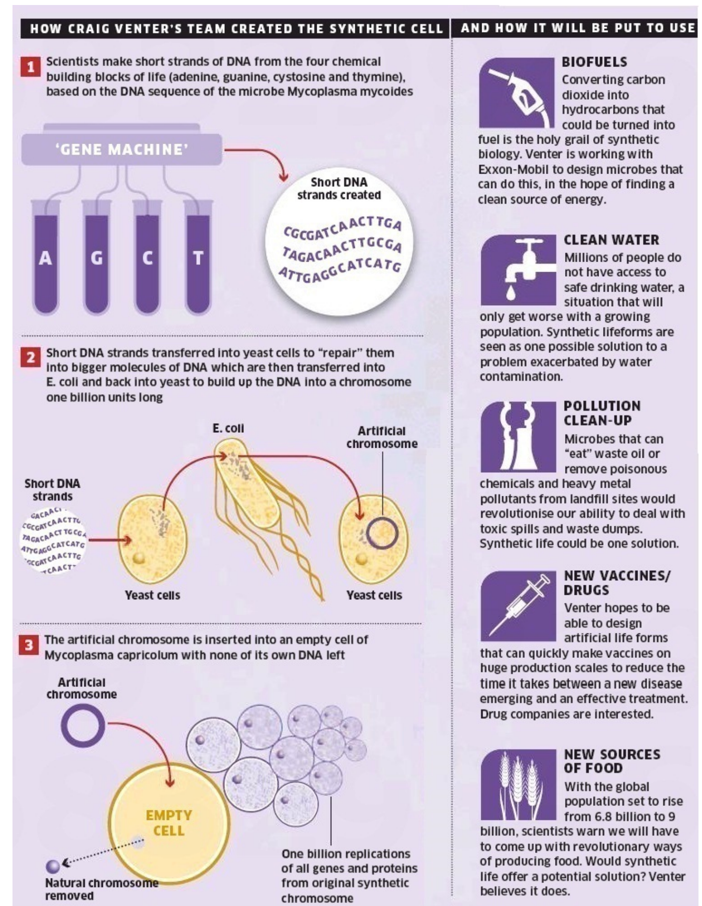
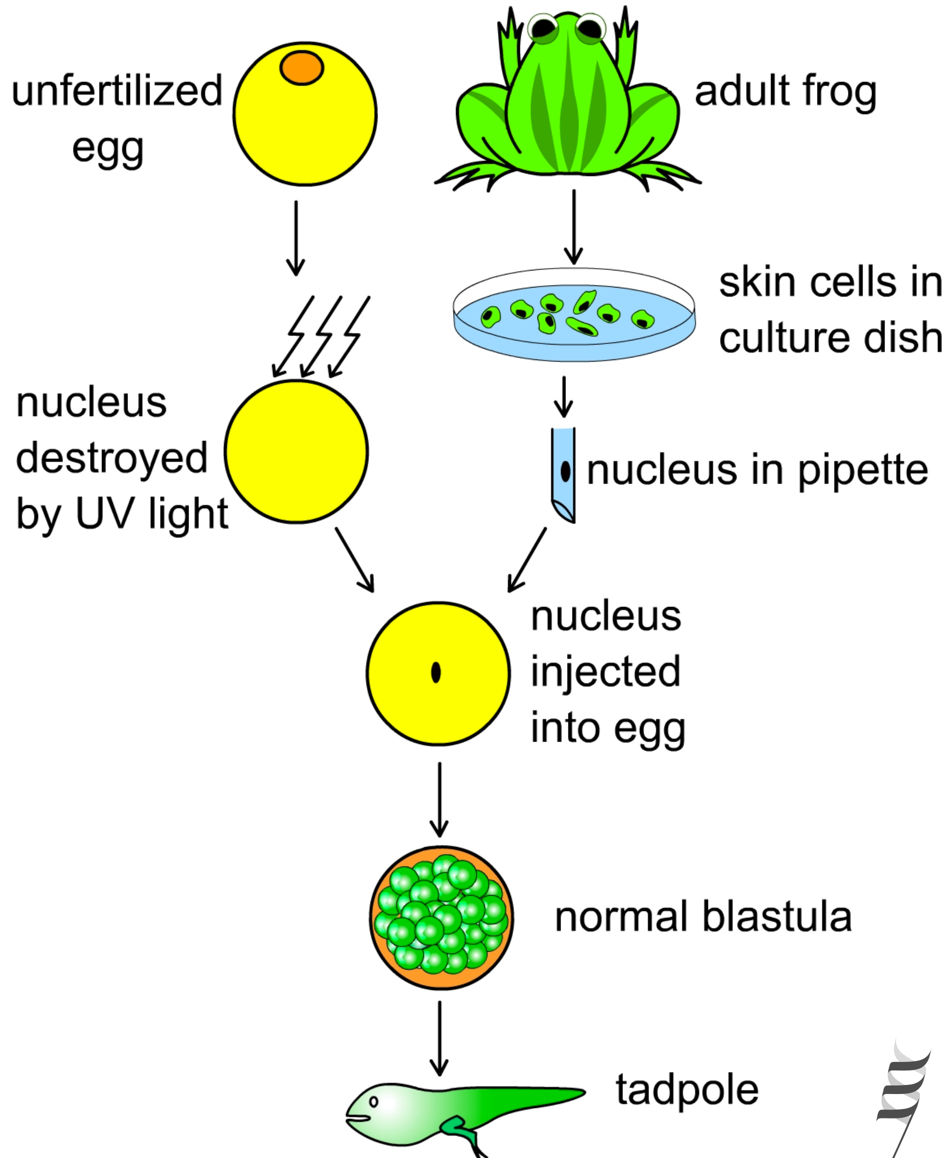


Figure 1



Experiments: green skin to froggy

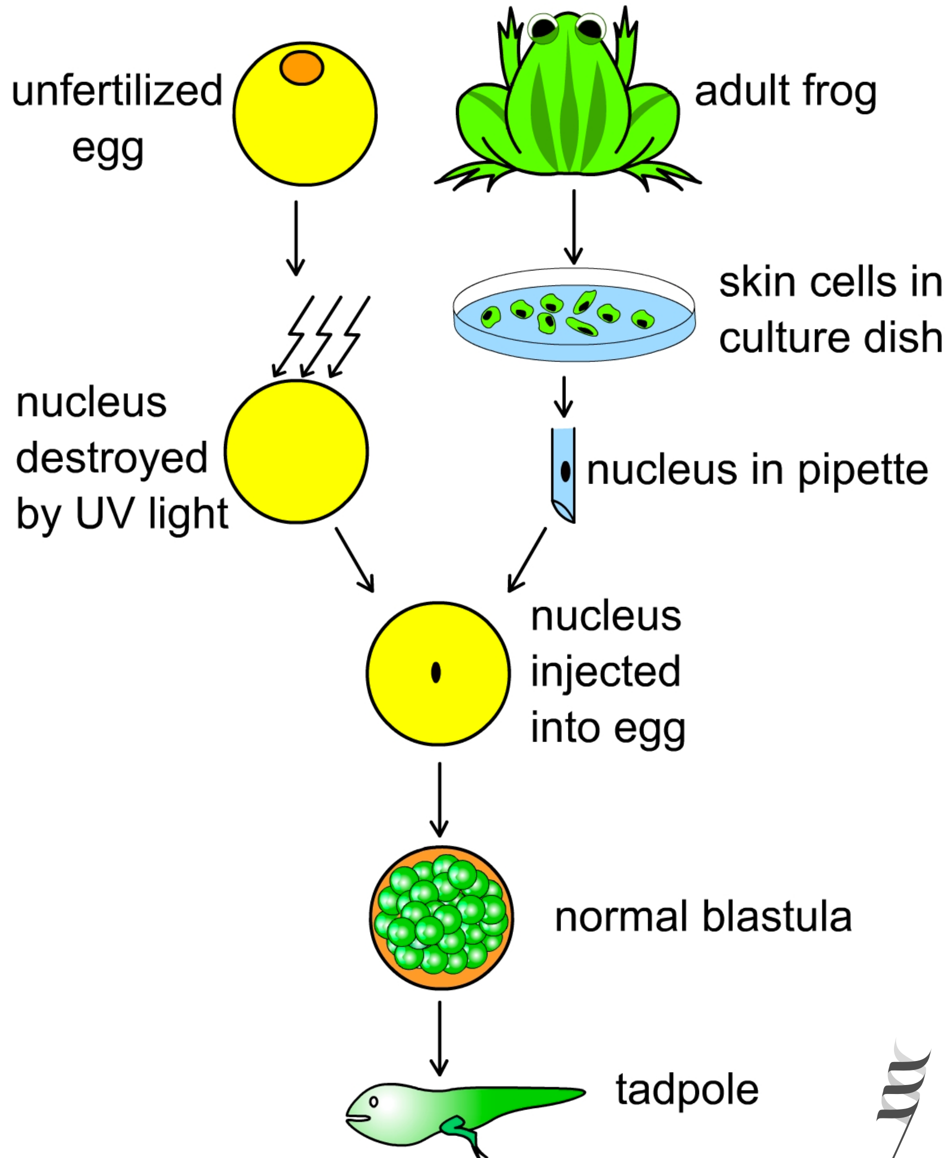
- Take skin cells and remove the nucleus.
- **Skin cells are differentiated. Correct?**
- Take unfertilized egg and remove the chromosomes. **You now have empty egg**.



Experiments: green skin to froggy

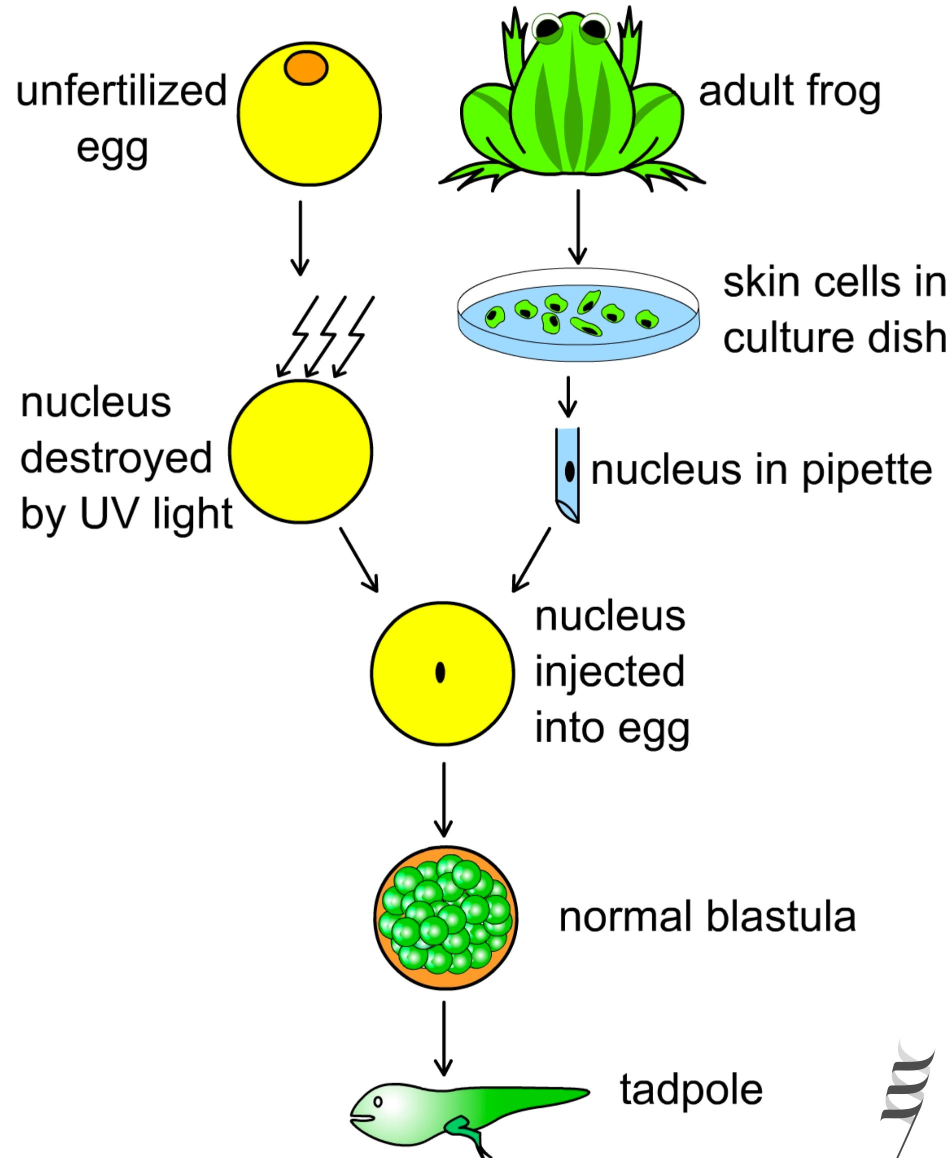
- Take the nucleus of the skin cell (chromosomes) and put them in the empty egg.

- Let it grow.

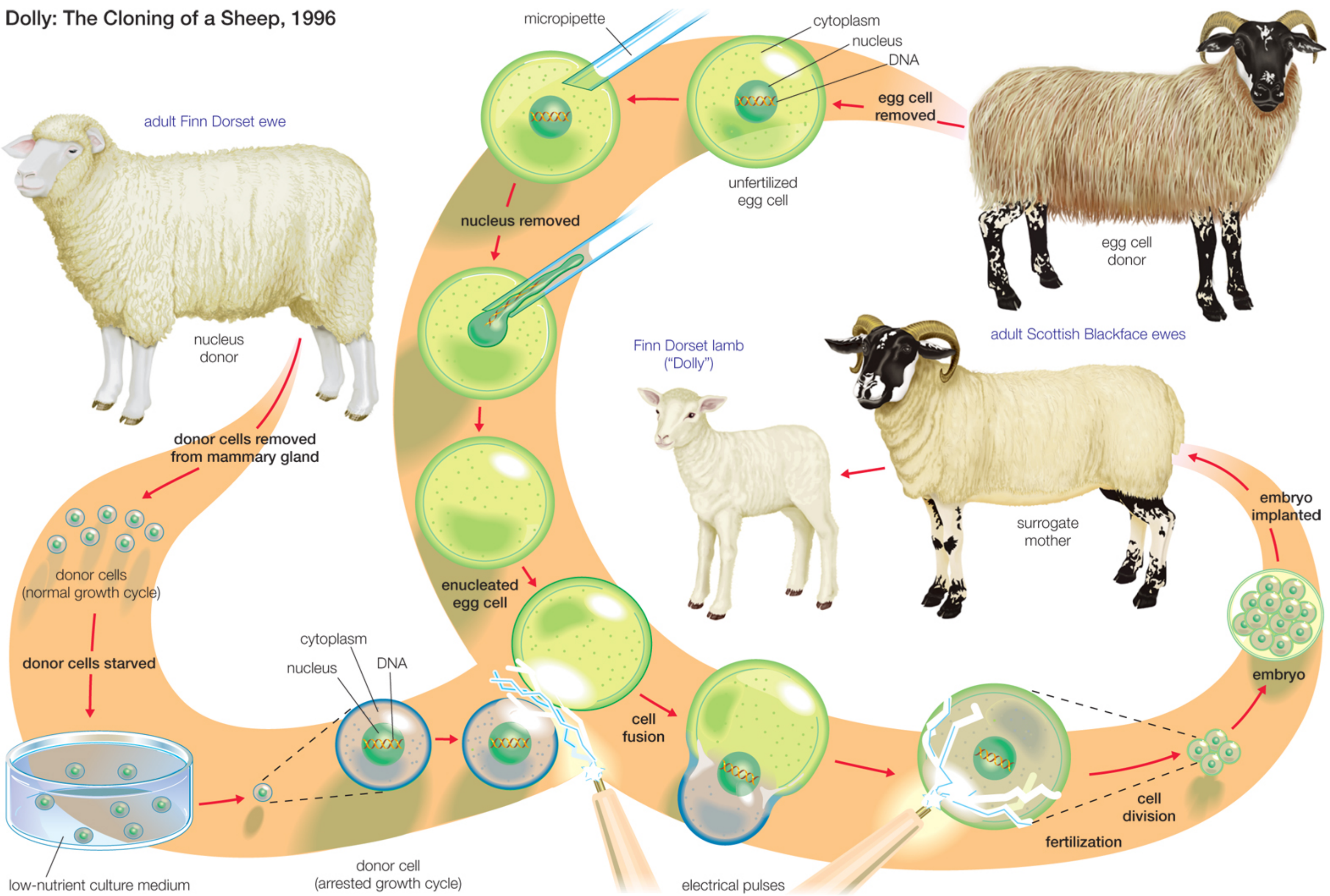


Experiments: green skin to froggy

- The cell will grow into a full organism.
- **Conclusion:**
  - **The genes in the skin cell can regenerate all other types of cells.**
  - **Genes are the same.**



Experiments: Dolly the sheep



Overview

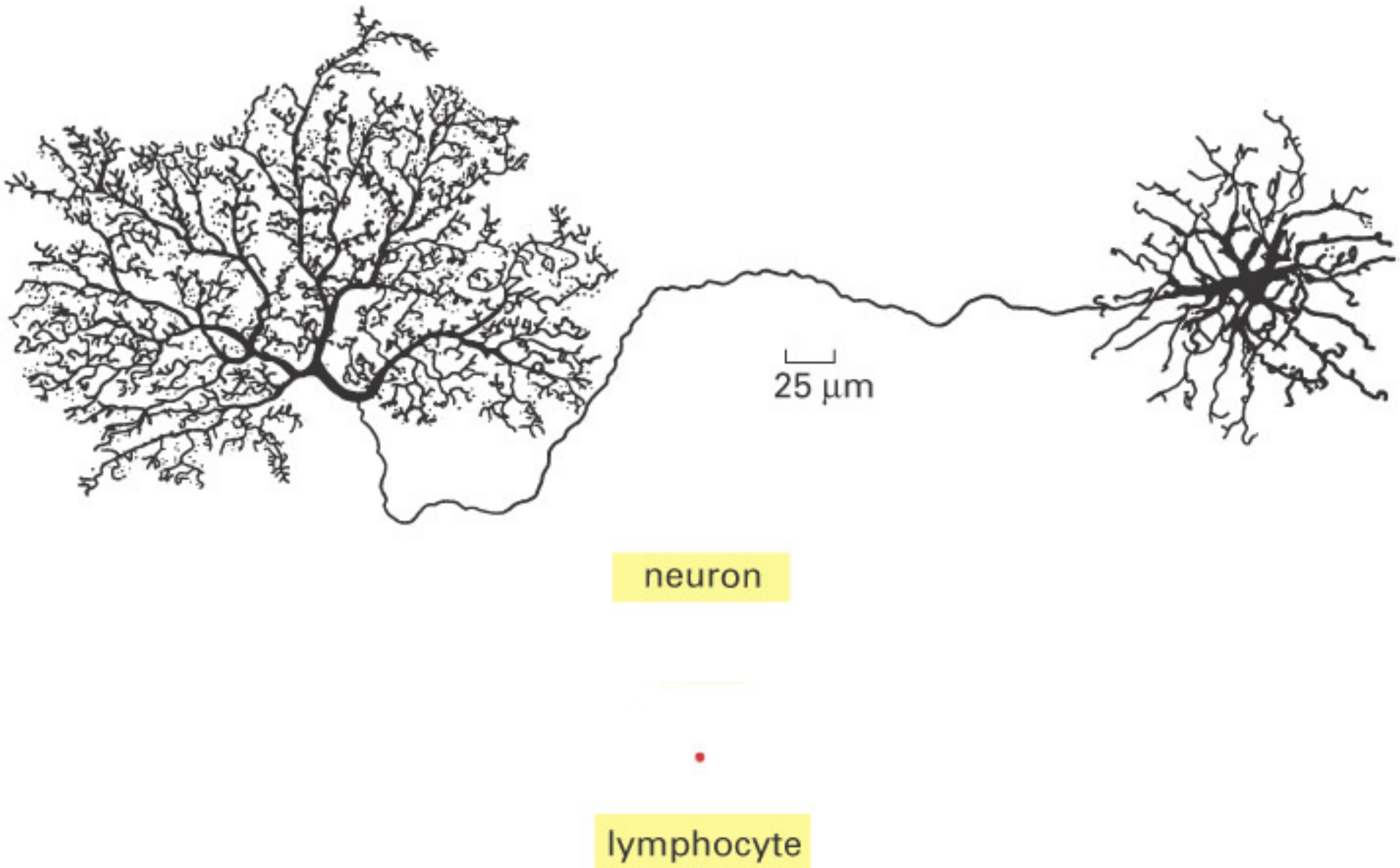
- Consider the differences between a nerve cell and a lymphocyte.

- Both cells have the same genome.

- **But they differ in:**

  - Size
  - Shape
  - Function

Overview



Overview

What are the conditions to make one specific product?

When to express one gene or another?

What mechanisms control gene expression?

General statements

- Many processes in the cell are the same across different types of cells.
- Thus cells have the same genes expressed and proteins/RNA made.
- These genes maintain the basic functions of the cell.

General statements

Examples:

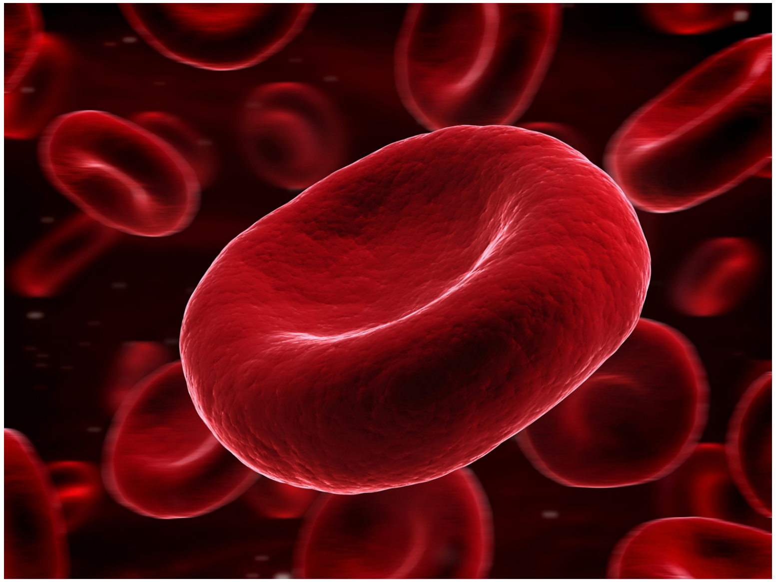
RNA polymerase - DNA repair enzymes
Ribosomal proteins – rRNA – tRNA – Etc.

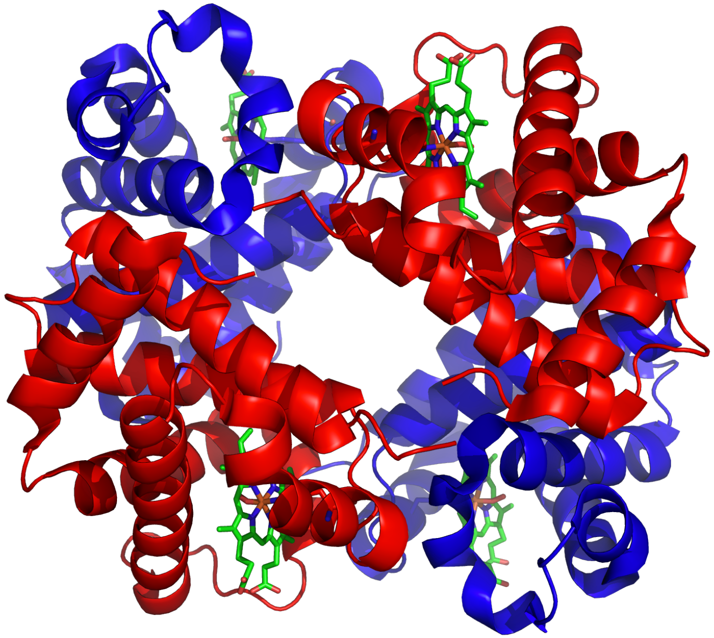
- These genes are called **housekeeping genes or constitutive genes.**
- These genes are switched **ON** almost all the time.

General statements

- Some proteins are found only in a specific specialized cells and not in any other cells.
- **Example:** Hemoglobin is found only in red blood cells.
- Such genes are referred to as **regulated genes.**
- These genes gets switched **ON** and **OFF** depending on the need and location (cell type).

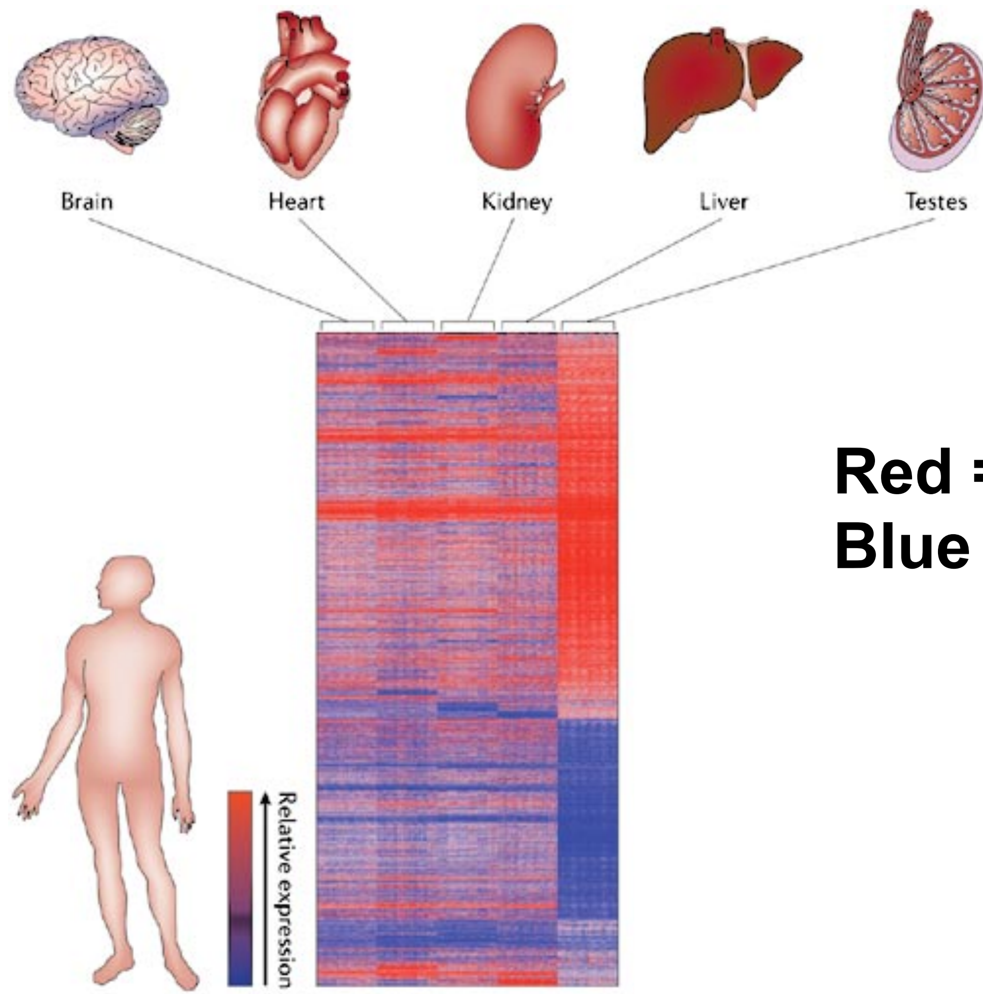
General statements





General statements

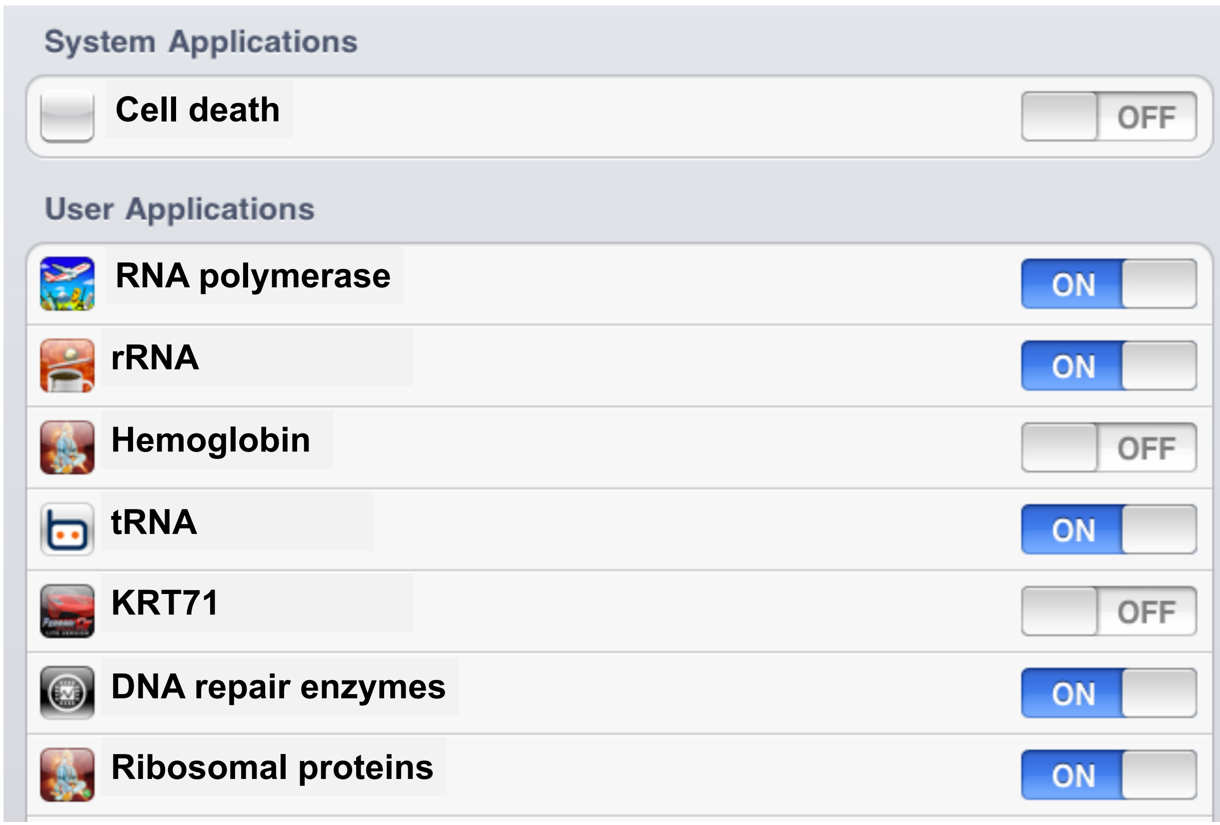
Levels of expression of mRNA (# of genes switched **ON**) is different depending on location and time



Red = gene ON
Blue = gene OFF

Gene expression

Regulation of gene expression is simply turning genes ON and OFF as needed

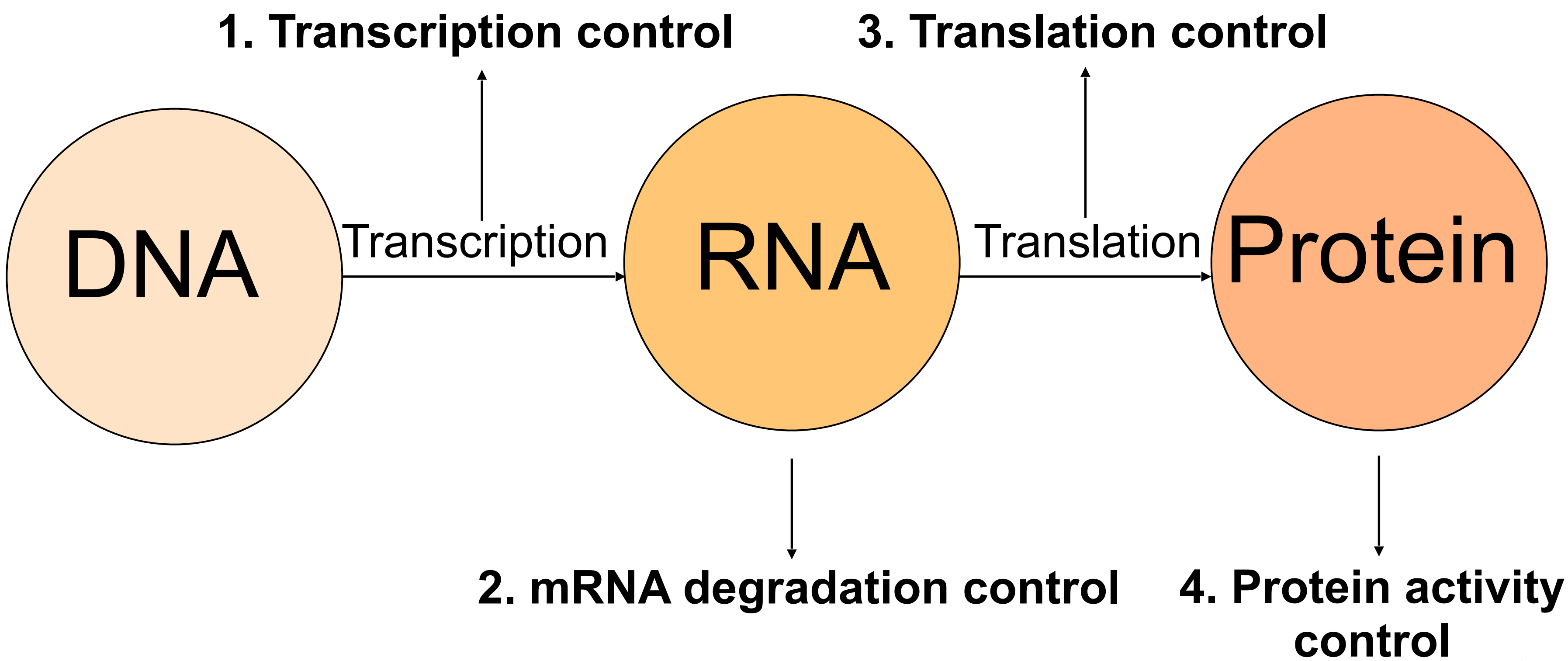


Gene expression

When in the pathway of gene expression regulation takes place?

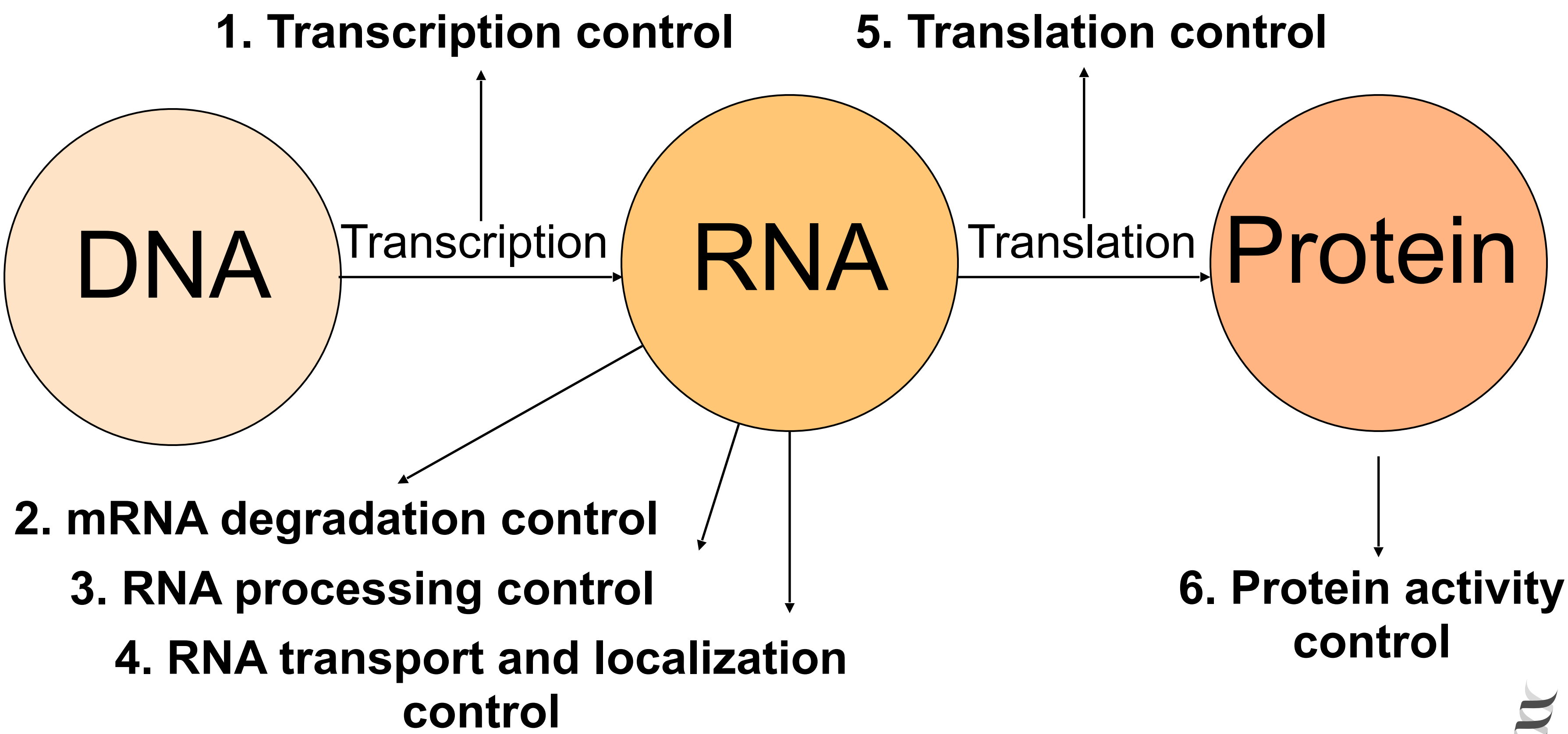
Regulation of Gene expression

Prokaryotes: regulation of gene expression can take place at multiple stages during the transcription/translation process.



Regulation of Gene expression

Eukaryotic: regulation of gene expression can take place at multiple stages during the transcription/ translation process.



Regulation of Gene expression

- **Transcriptional control:** controlling when and how often a gene is transcribed.
- **RNA processing control:** controlling how a transcript is being spliced or processed.
- **mRNA degradation control:** selectively choosing mRNA in the cytoplasm for destabilization and degradation.
- **RNA transport and localization**: controlling which mature mRNA leaves the nucleus to the cytoplasm and where.

Regulation of Gene expression

- **Translational control:** controlling which mRNA in the cytoplasm gets translated by ribosomes.

- **Protein activity control:** selectively choosing a protein for activation, inactivation, or degrading.

1.Transcriptional control

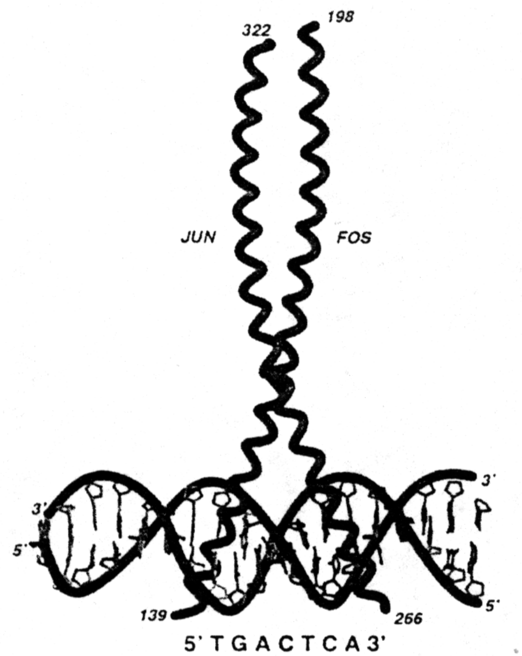
- Transcription control is achieved by molecular/ genetic switches.
- Genetic switches that control transcription are composed of:

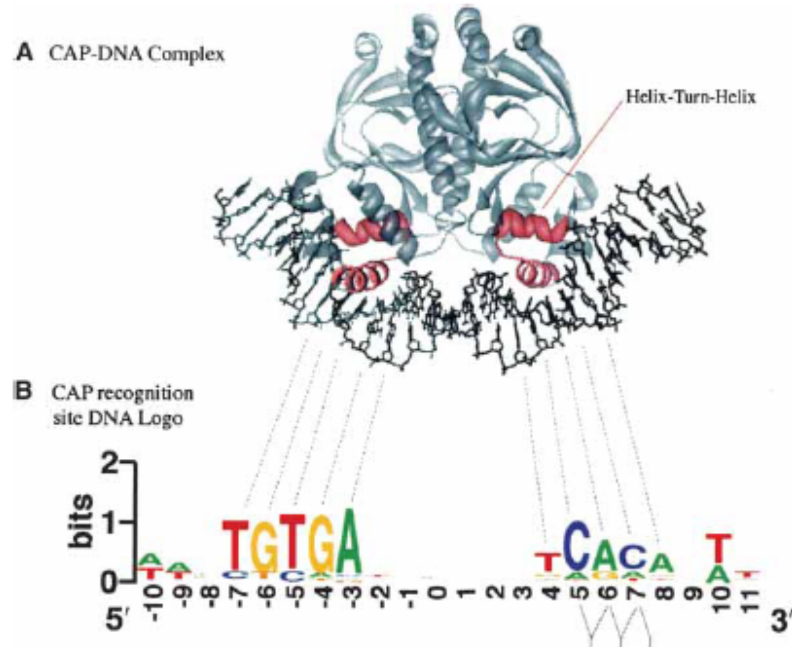
1. **DNA motif**: specific DNA sequence that gets recognized by specific regulatory proteins.
2. **Proteins**: proteins that binds to specific DNA sequence to affect transcription.

1.Transcriptional control – DNA motif

- The DNA motif size and nucleotide composition depends on the protein that is associated.
- Each class of proteins has a general motif structure and sequence.
- The motif sequence is specific and **NOT** every regulatory protein can recognize it.

1.Transcriptional control – DNA motif





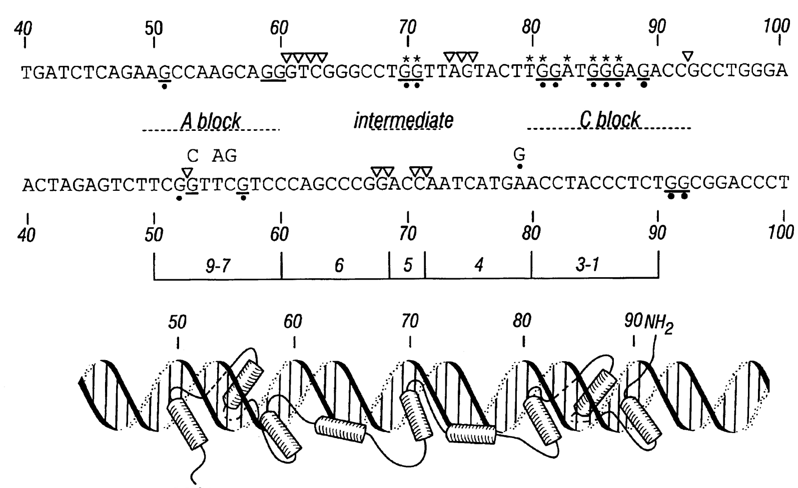


FIG. 1

1.Transcriptional control – regulatory proteins

Regulatory proteins belong to multiple classes.

The different classes have specific protein structure and recognizes specific motifs.

Regulatory proteins:

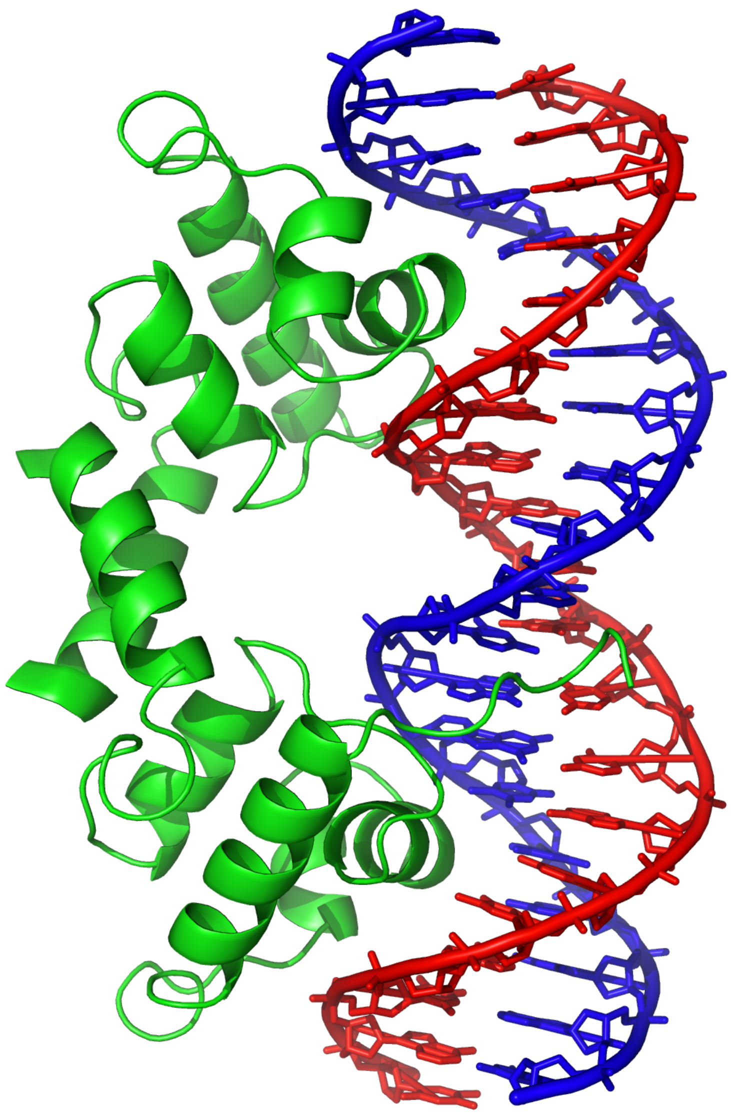
Helix turn helix

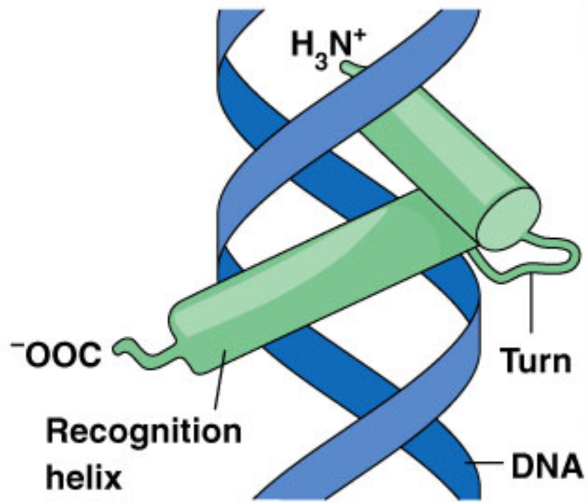
Helix loop helix

Leucine zipper

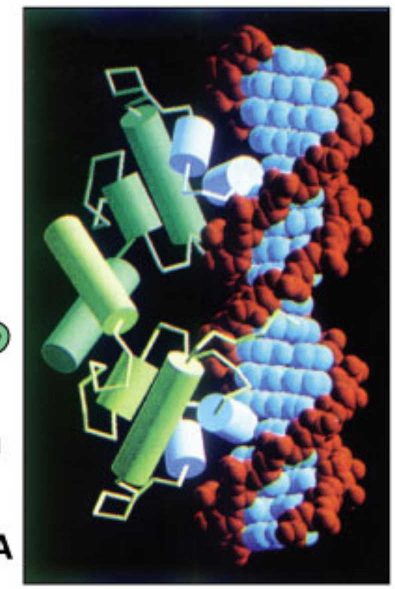
Zinc fingers

Switch 1: helix turn helix + motif



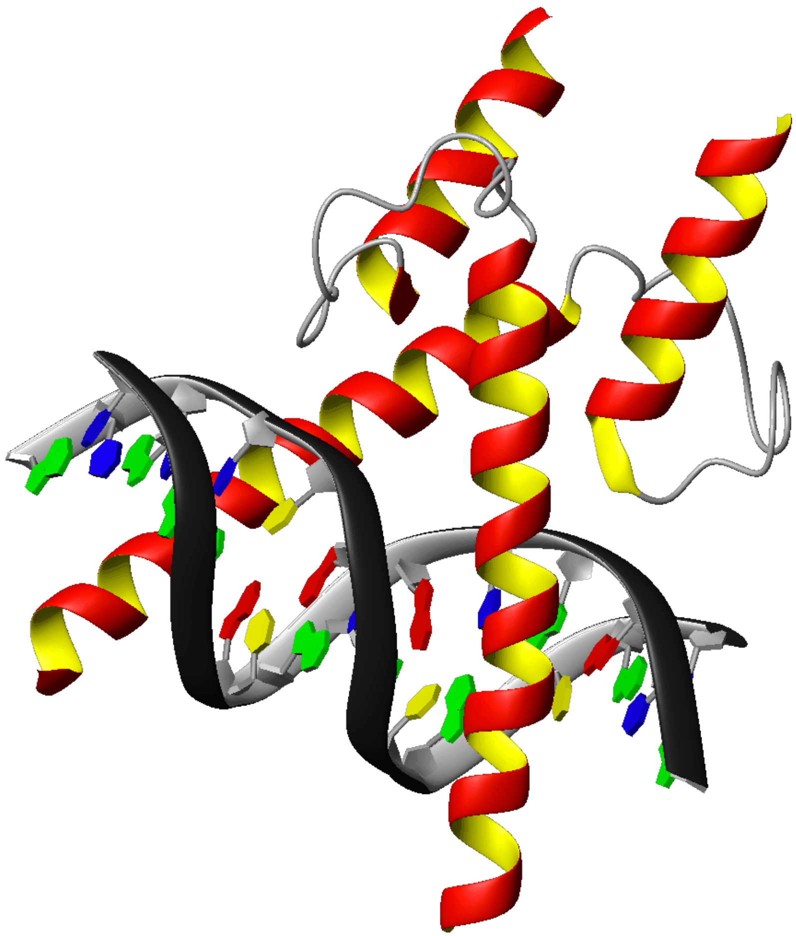


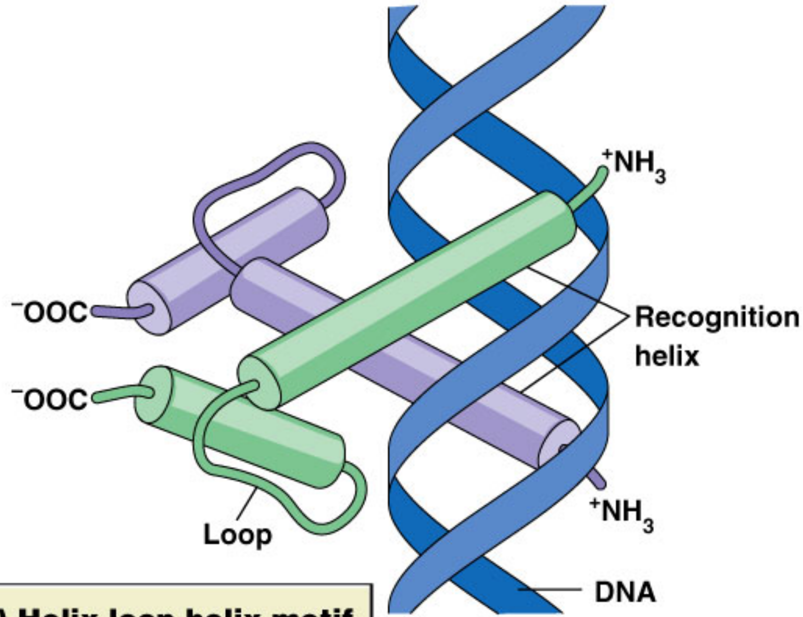
(a) Helix-turn-helix motif



Phage λ repressor bound to DNA

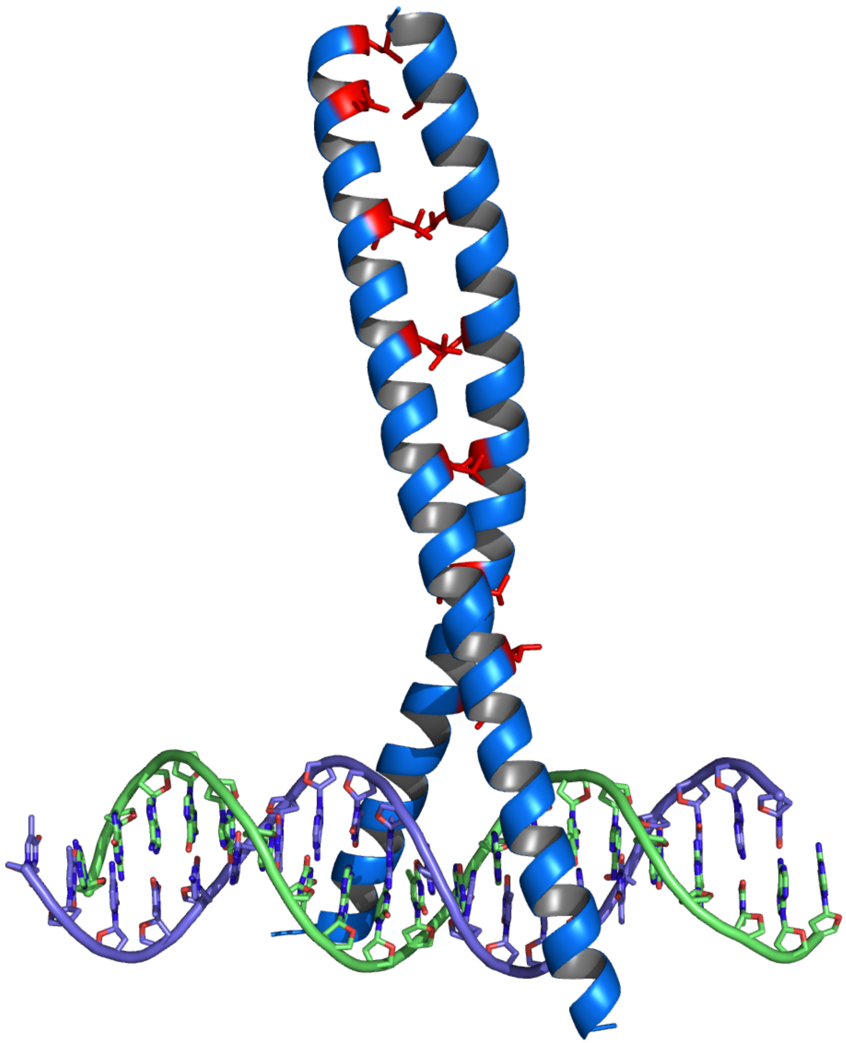
Switch 2: helix loop helix + motif

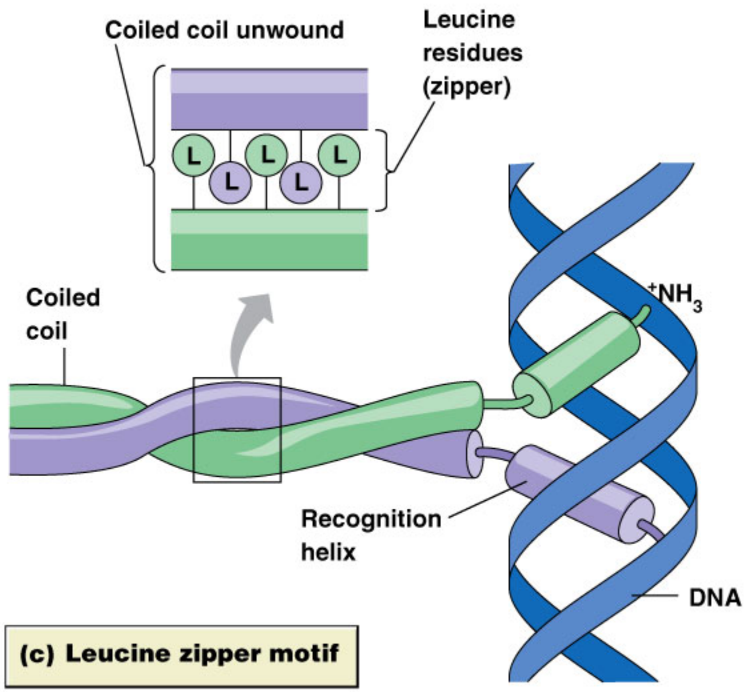




(d) Helix-loop-helix motif

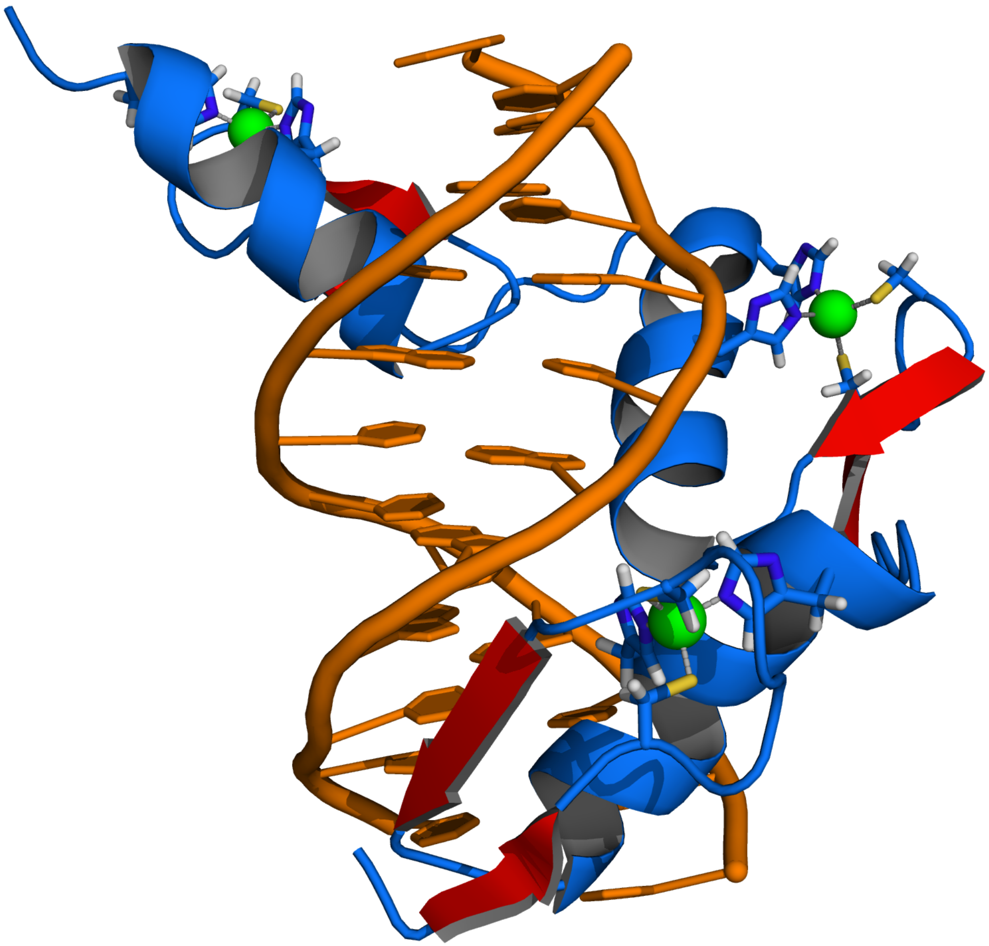
Switch 3: Leucine zipper + motif

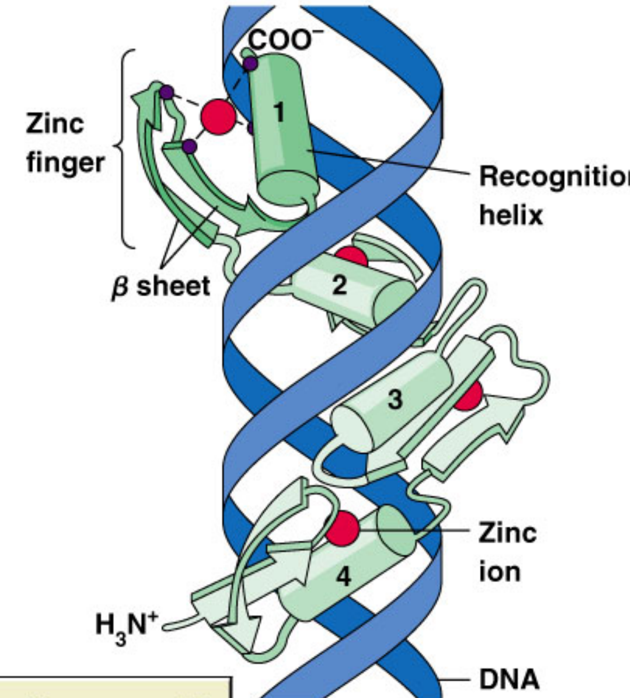




(c) Leucine zipper motif

Switch 4: Zinc finger + motif

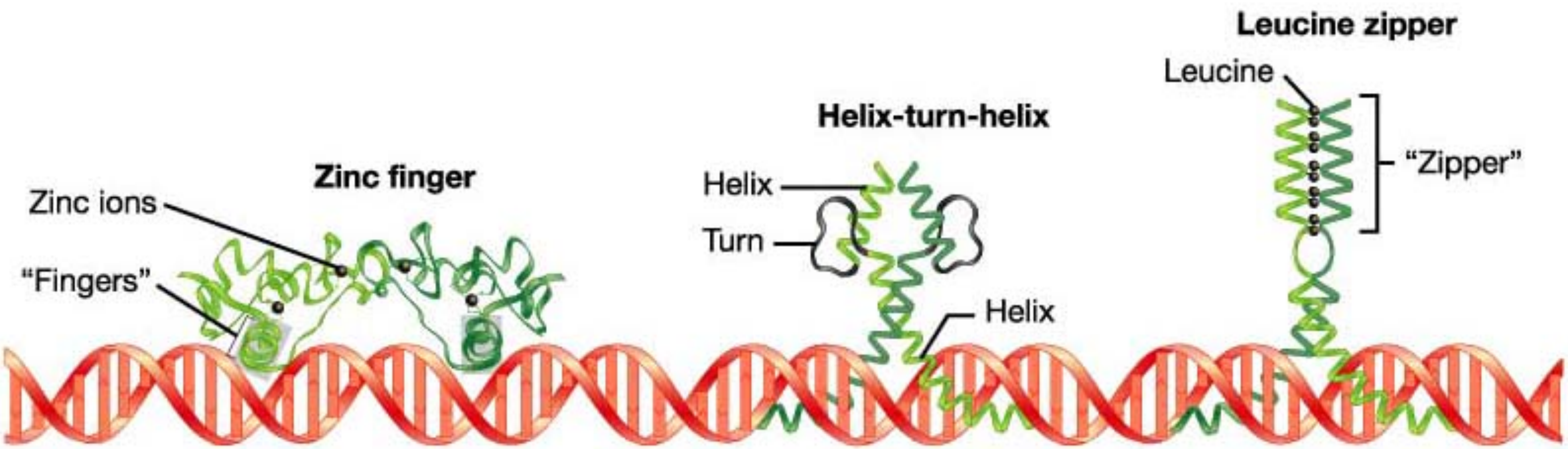




(b) Zinc finger motif

Summary

- Regulatory proteins recognizes specific regions near the gene.
- The binding of the regulatory proteins to the DNA motif may turn gene on or off and thus fulfilling its purpose as a genetic switch.



To know

How cells differ in shape, size, and function?

Cell differentiation depends on?

Translation control

Transcription control

Helix-turn-helix

Cloning experiment

RNA transport and localization control

RNA processing control

Zinc finger

Helix-loop-helix

Regulated genes

Leucine zipper

Constitutive genes

Housekeeping genes

Regulatory proteins

DNA motif

mRNA degradation control

Protein activity control

Expectations

- You know the significance of gene expression control for cells/organisms.
- You know the places where control of gene expression can take place.
- You know the DNA motifs and the different classes of regulatory proteins.

For a smile

READ THE SYLLABUS. READ THE SYLLABUS.
READ THE SYLLABUS. READ THE SYLLABUS.
READ THE SYLLABUS. READ THE SYLLABUS.