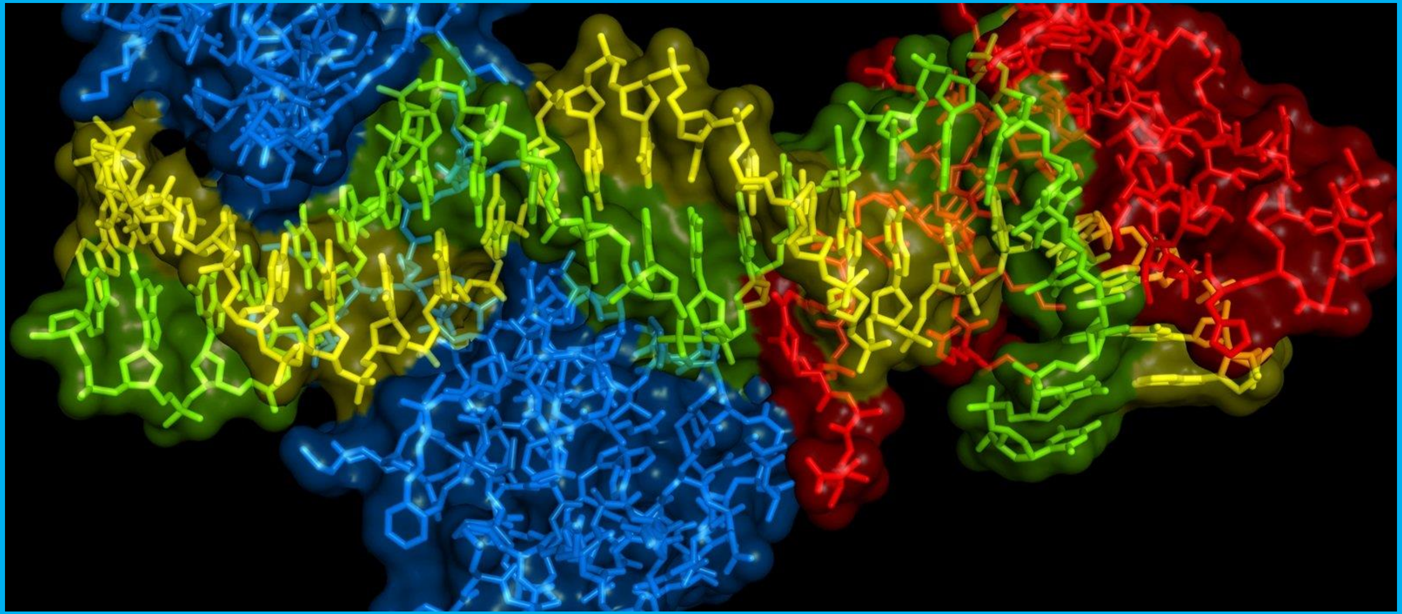
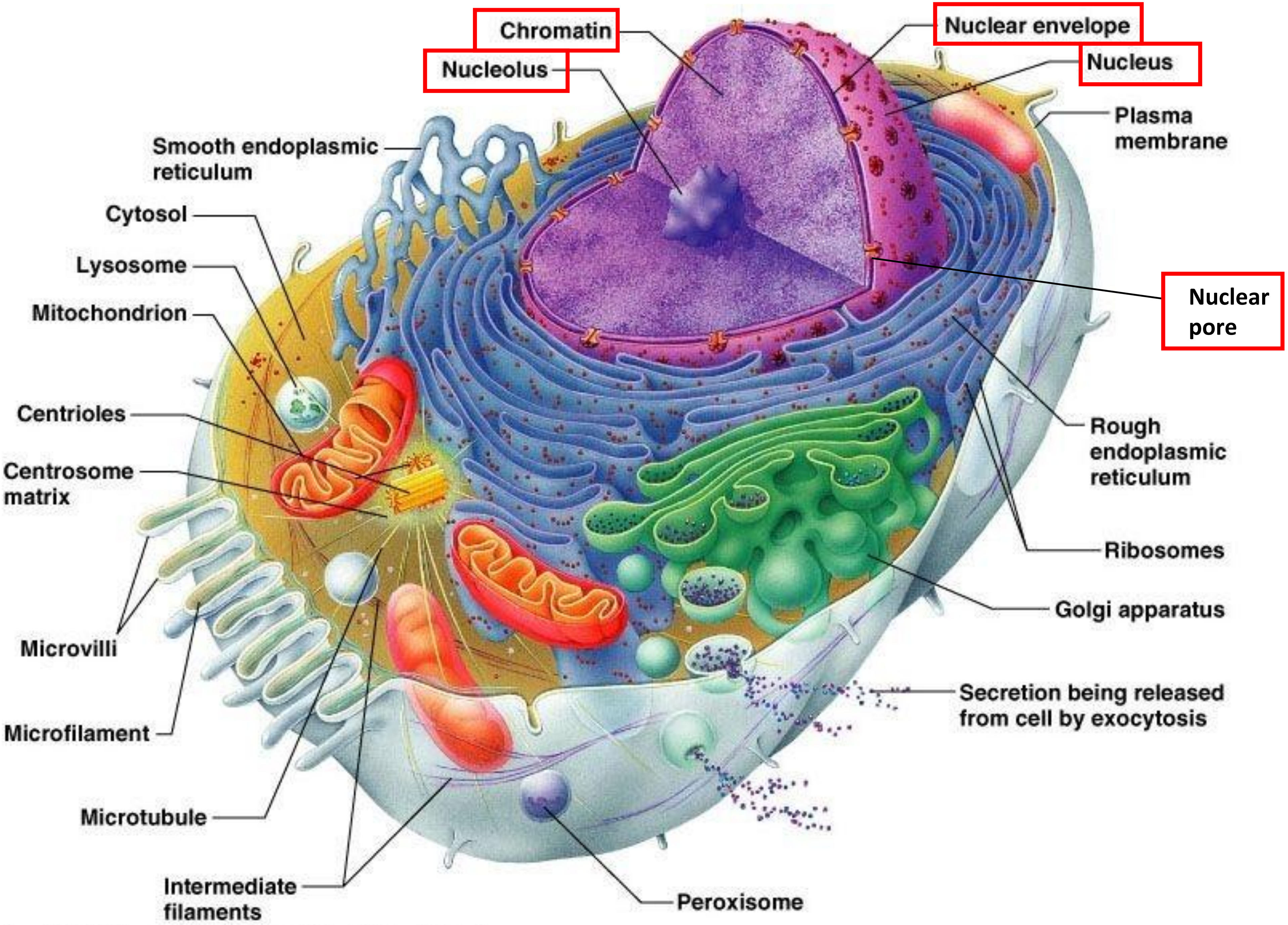


Nucleus and Gene Expression

Marjorie D. Shaw, Ph.D.

OLLI Fall 2023

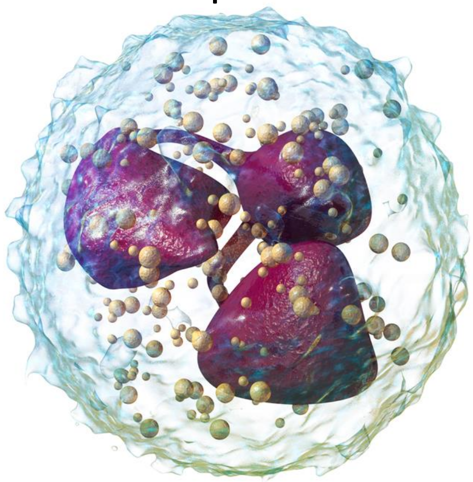
Study Group : 426

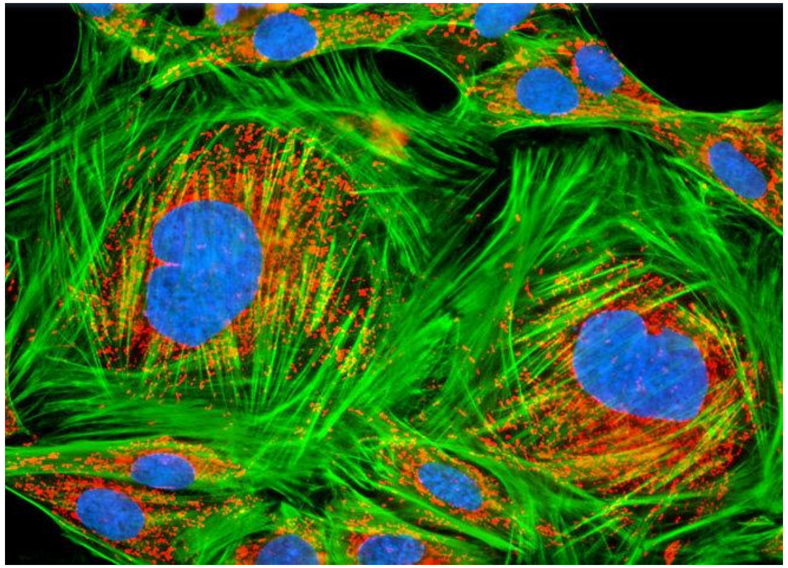

Chromatin
Nuclear envelope
Nucleolus
Nucleus
Plasma membrane
Smooth endoplasmic reticulum
Cytosol
Lysosome
Mitochondrion
Nuclear pore
Centrioles
Rough endoplasmic reticulum
Centrosome matrix
Ribosomes
Golgi apparatus
Microvilli
Secretion being released from cell by exocytosis
Microfilament
Microtubule
Intermediate filaments
Peroxisome

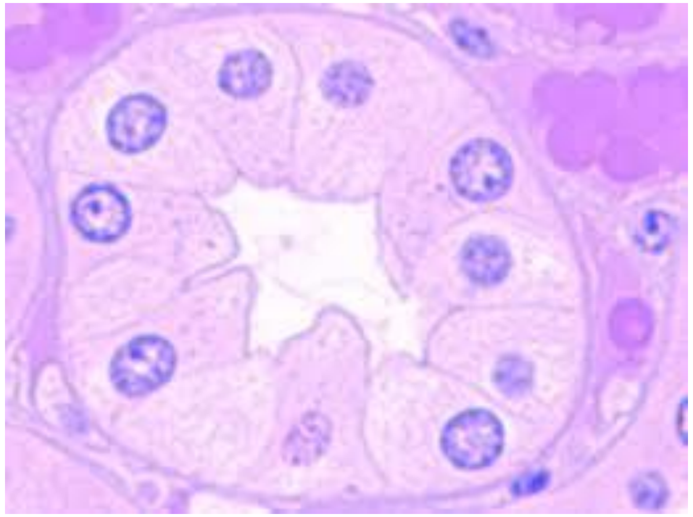
Nucleus

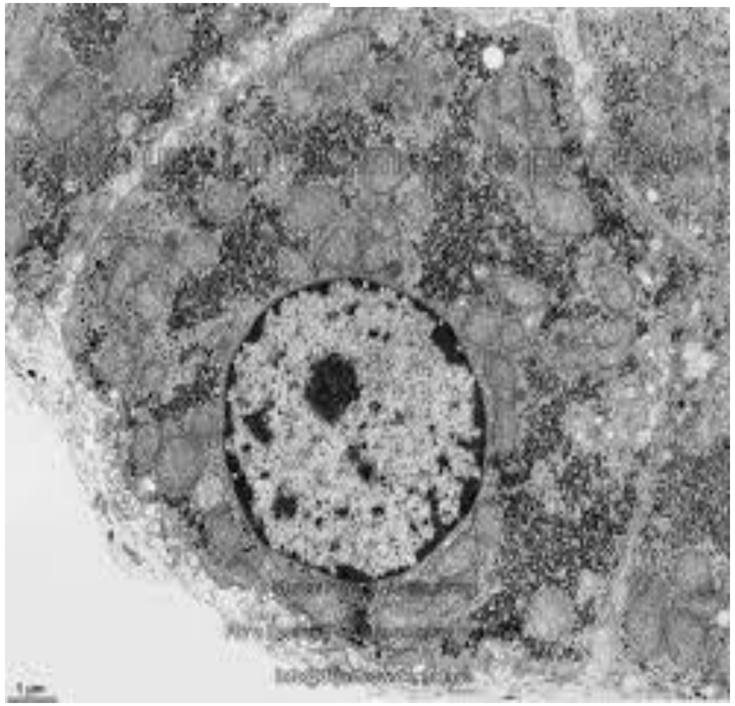
Largest organelle; membrane-bound, contains DNA in sequestered space. Defines all eucaryotic cells. Made of *nuclear envelope, chromatin and nucleolus*.

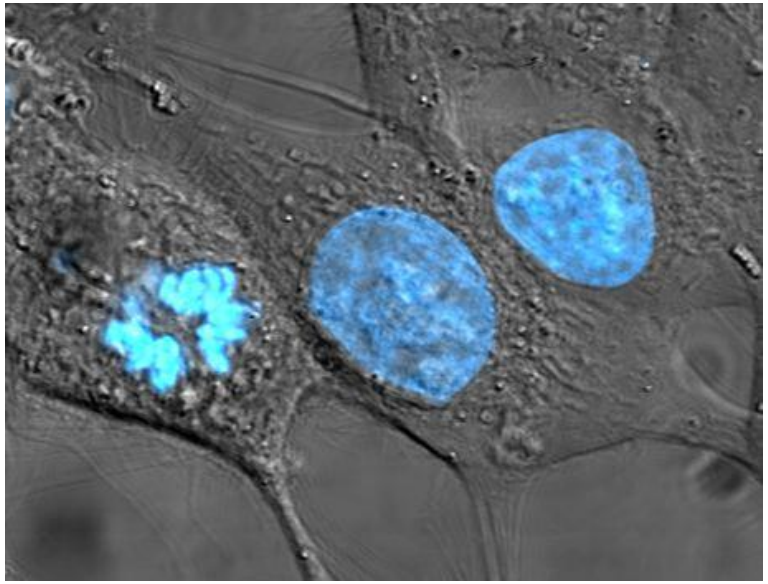
neutrophil





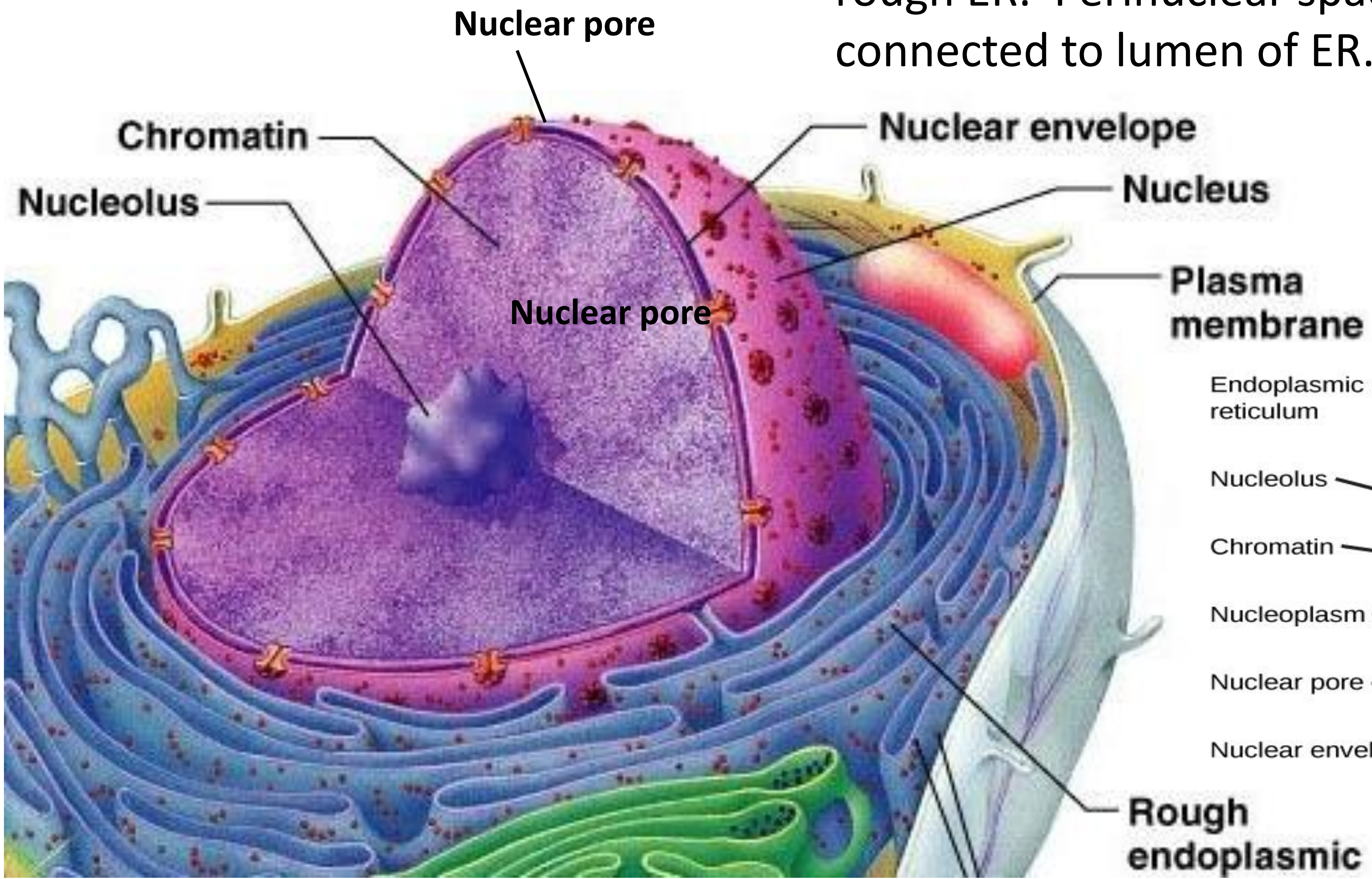


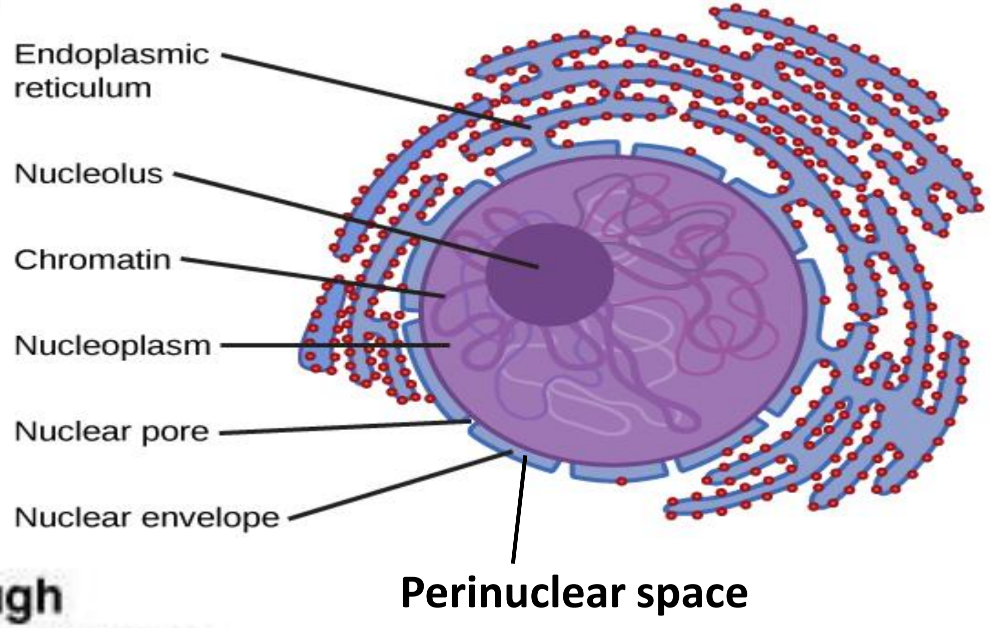




Nuclear Envelope

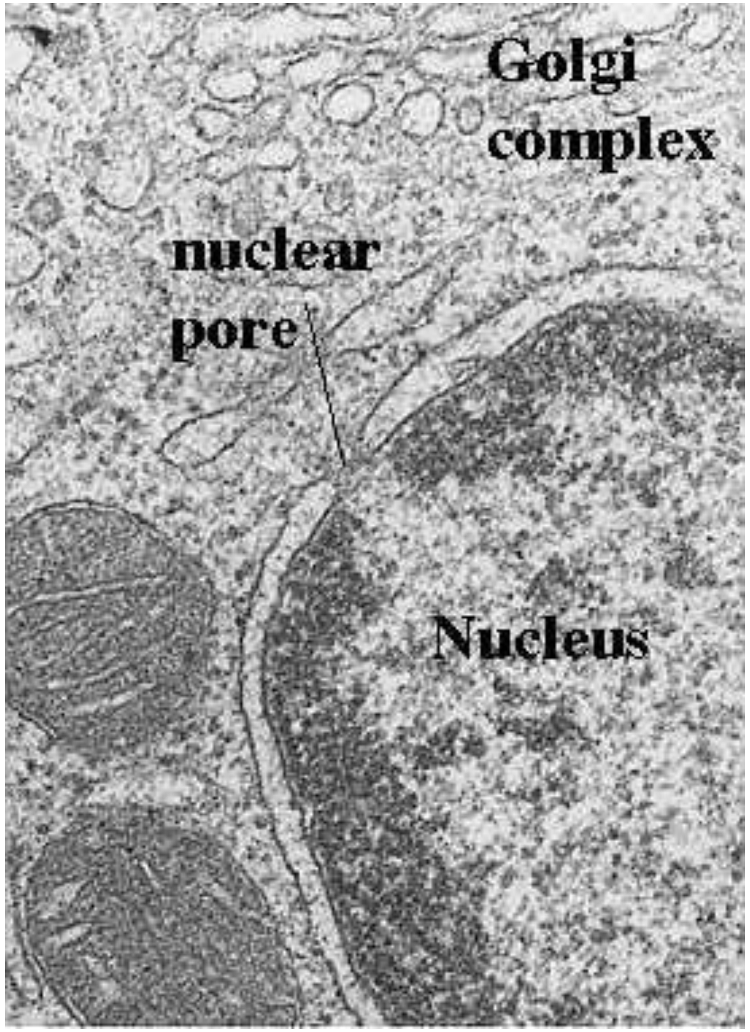
Double layer of bilaminar membrane, pierced with **nuclear pores** to regulate traffic. Outer layer connected with rough ER. Perinuclear space connected to lumen of ER.

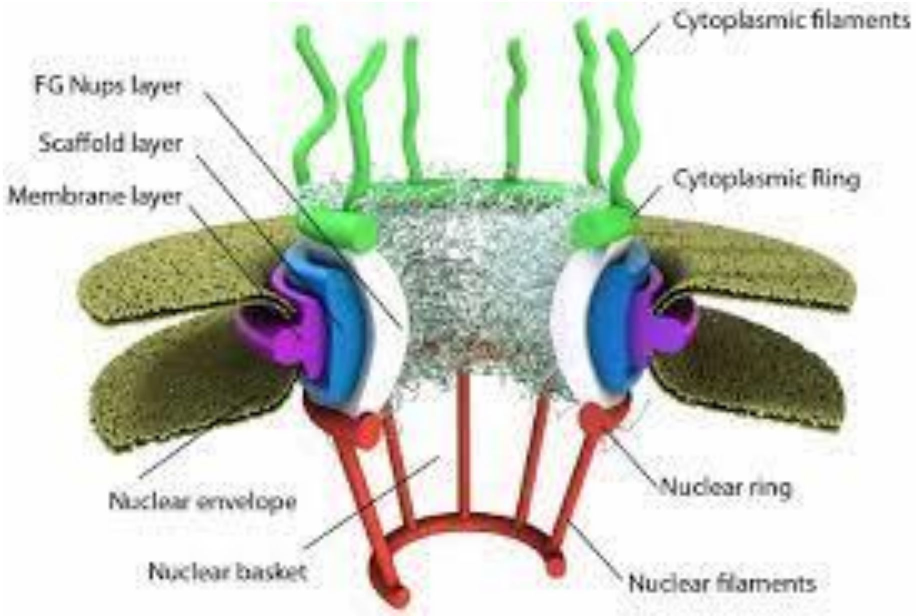


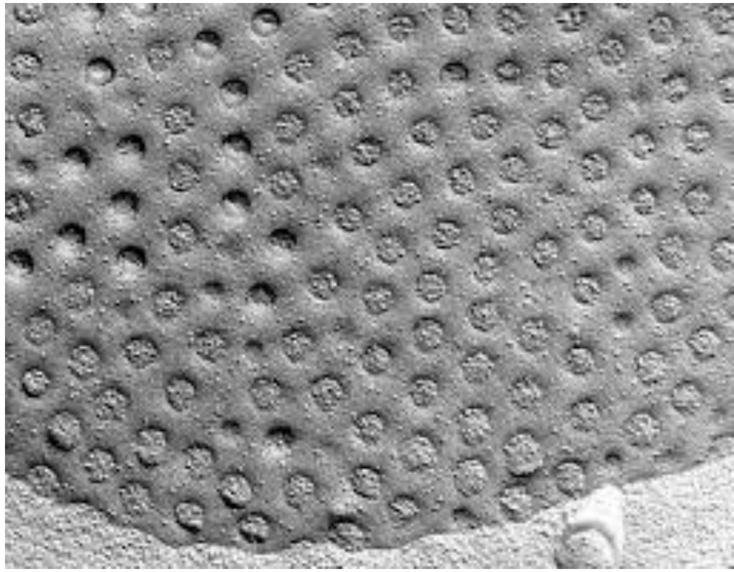


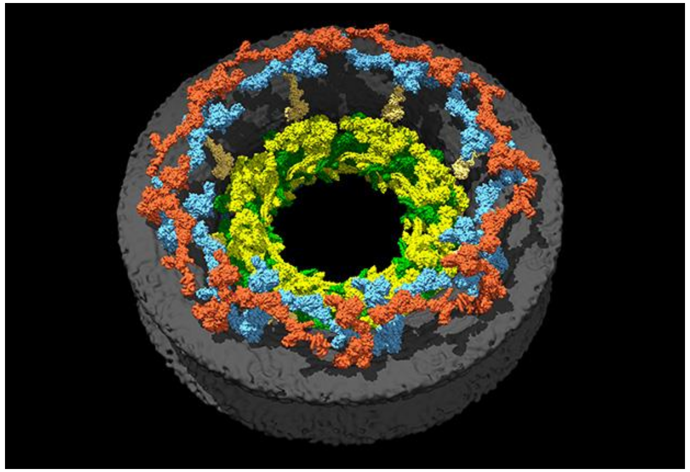
Nuclear pores

Complex nuclear pore complex (~50 proteins) control everything that goes in or out. Molecules must bear a special “tag” to allow them to pass.



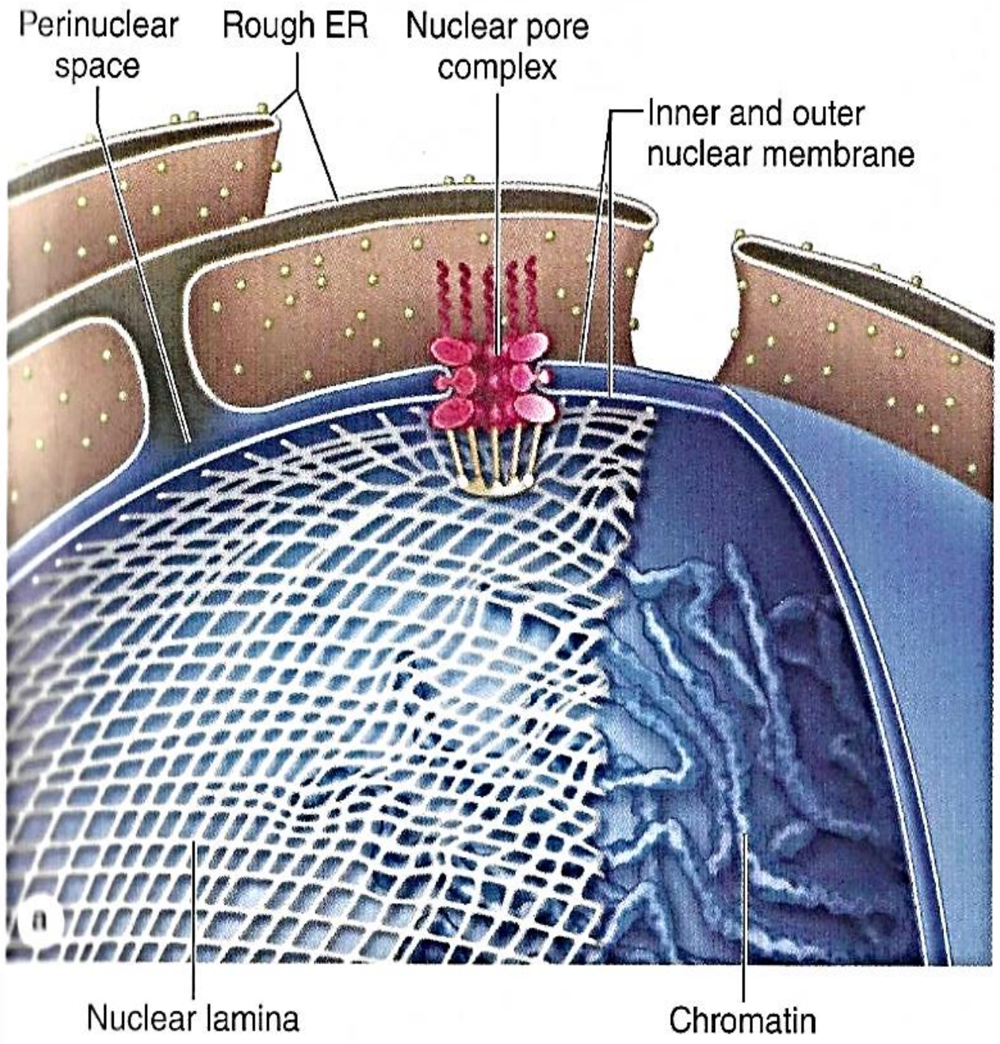


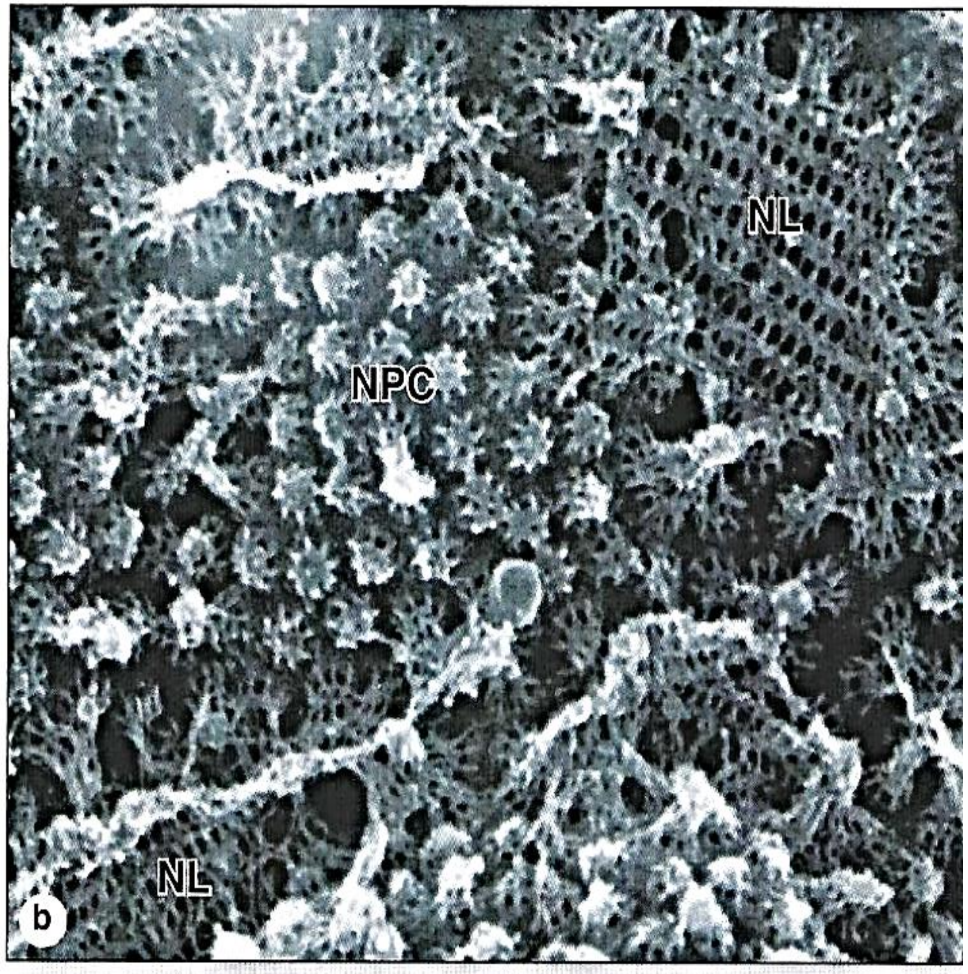




Nuclear lamina

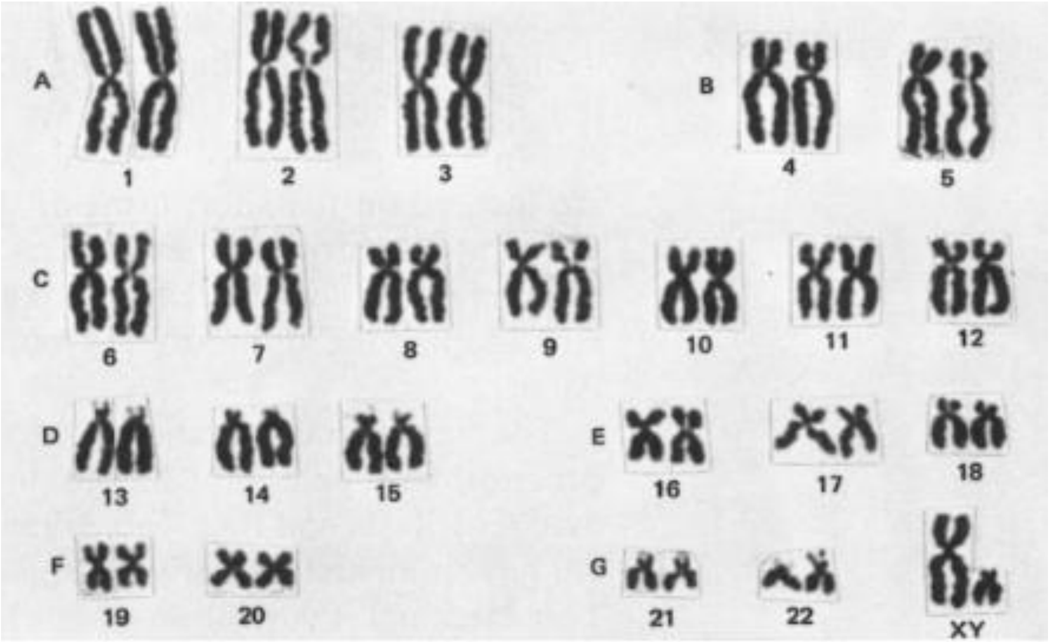
Network of intermediate filaments attached to inner membrane; reinforce nuclear envelope and anchor ends of the chromosomes



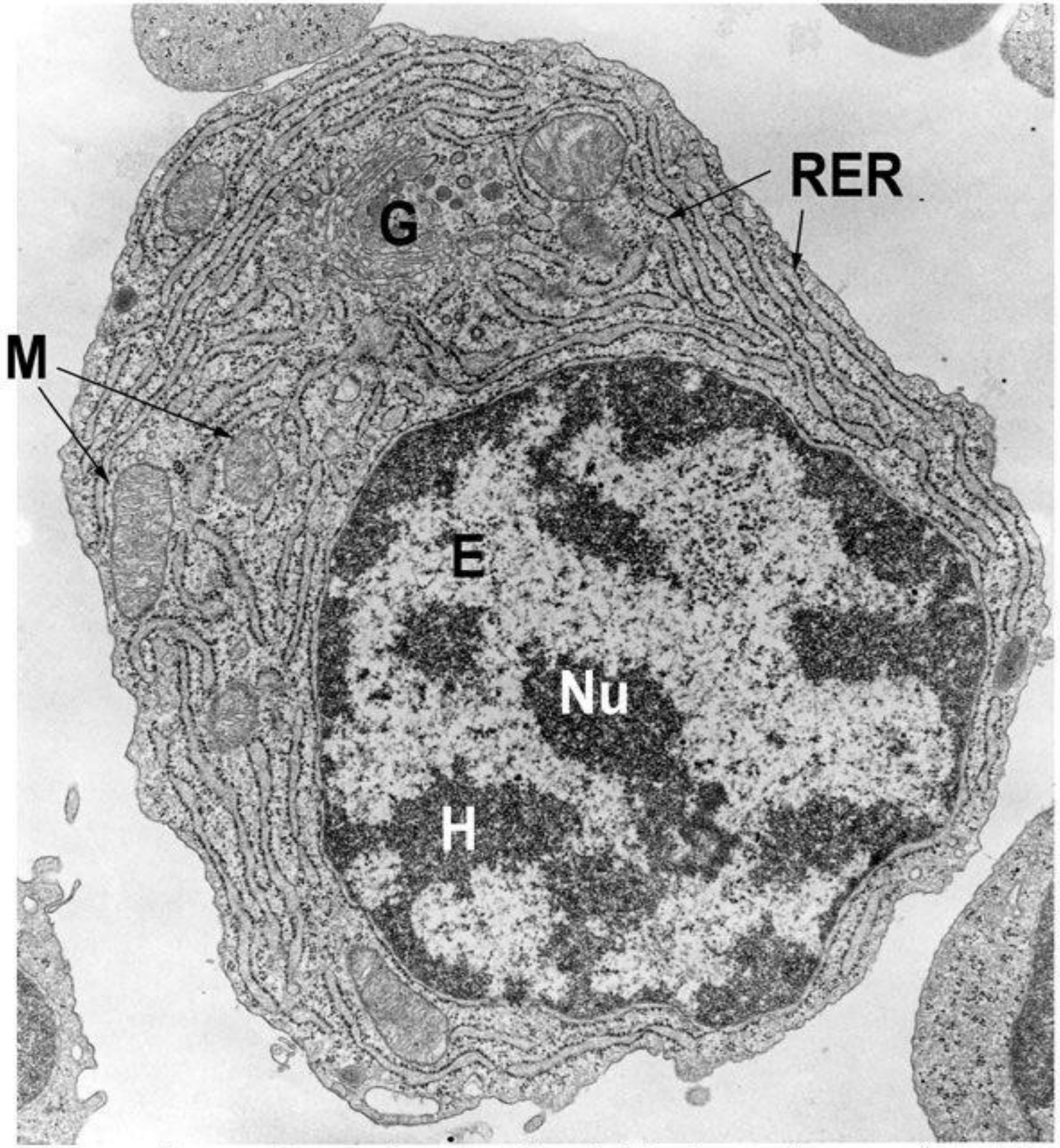


Chromatin

Chromatin = DNA + proteins. In working cell, active chromatin appears as dispersed **euchromatin**; inactive chromatin in denser **heterochromatin**.

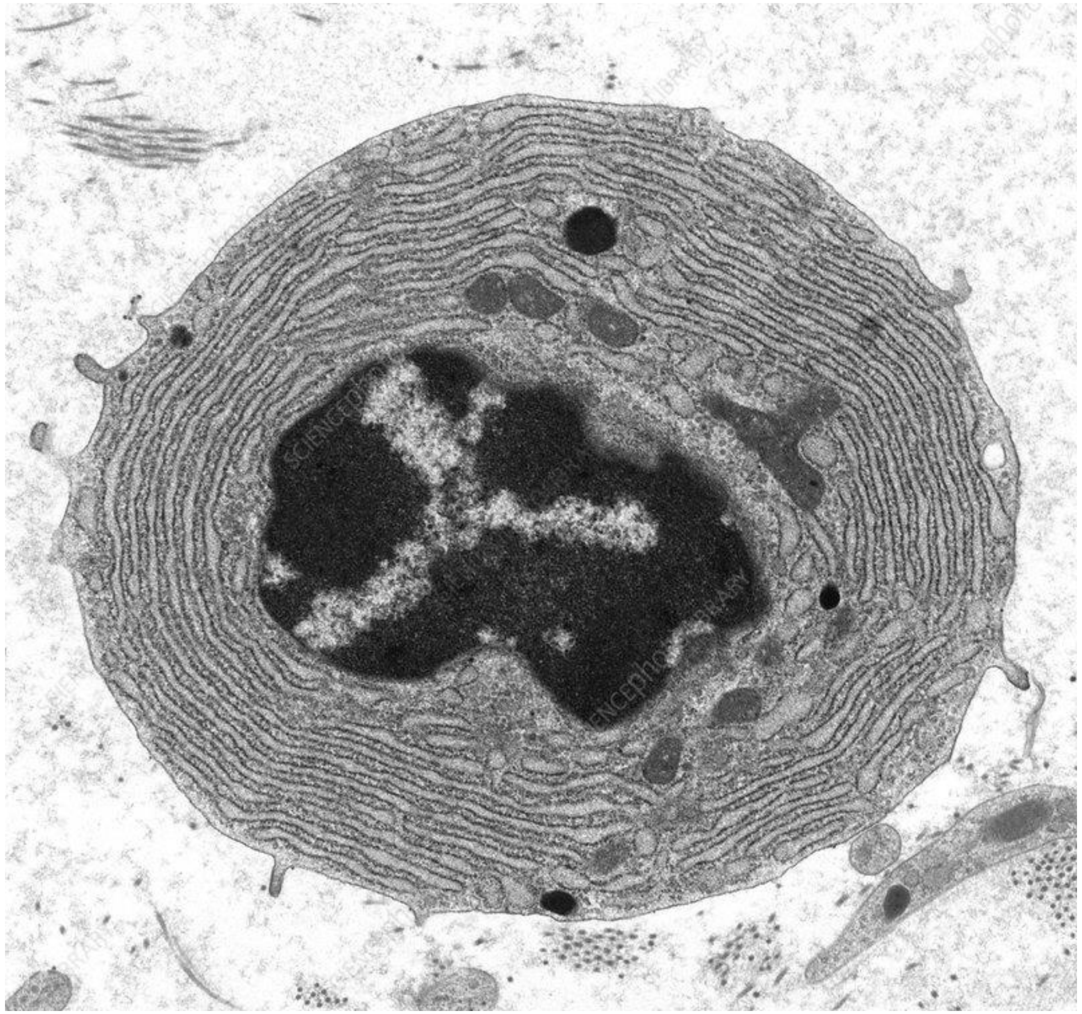


Karyotype: hyper-condensed chromosomes only visible in mitosis (cell division)

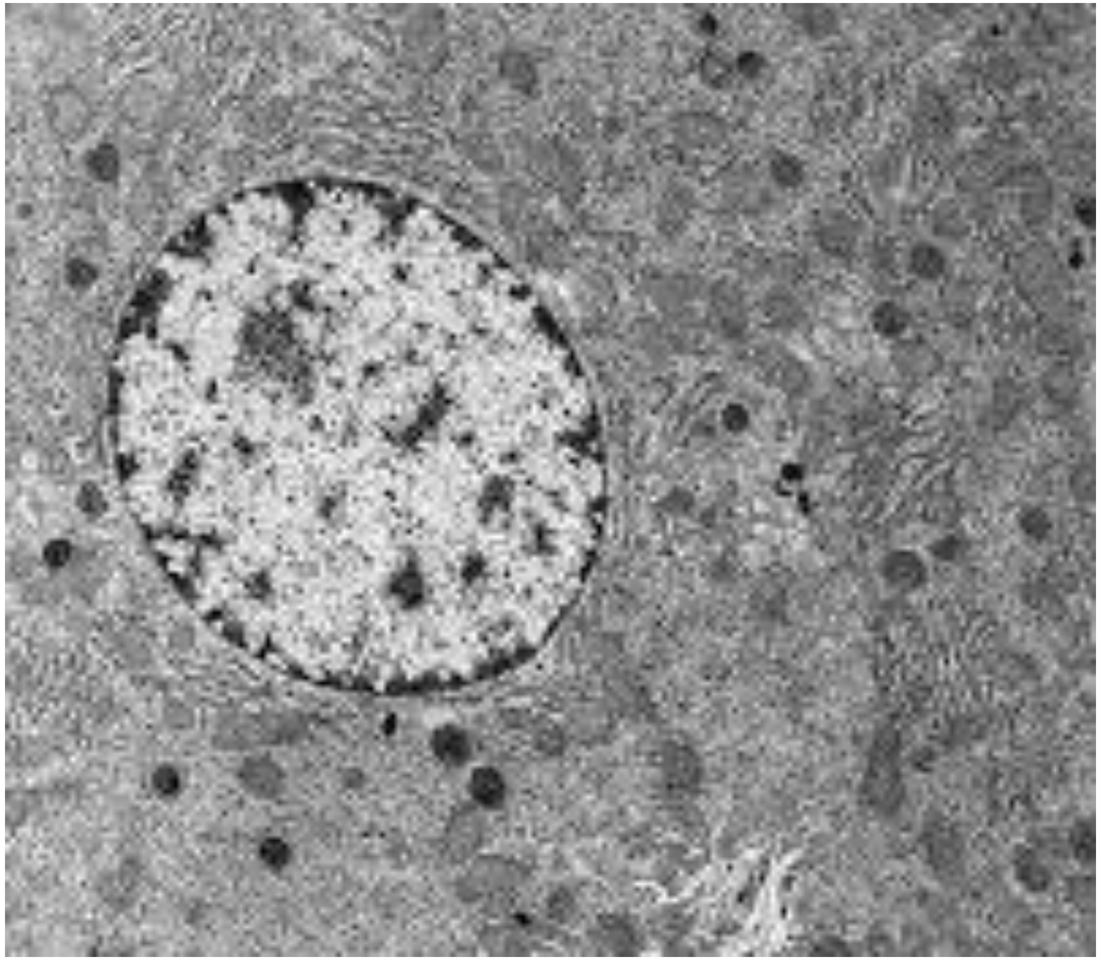


Nu-nucleus, E-euchromatin, H-heterochromatin, M-mitochondria, RER-rough endoplasmic reticulum, G-golgi complex

Chromatin reflects cell function

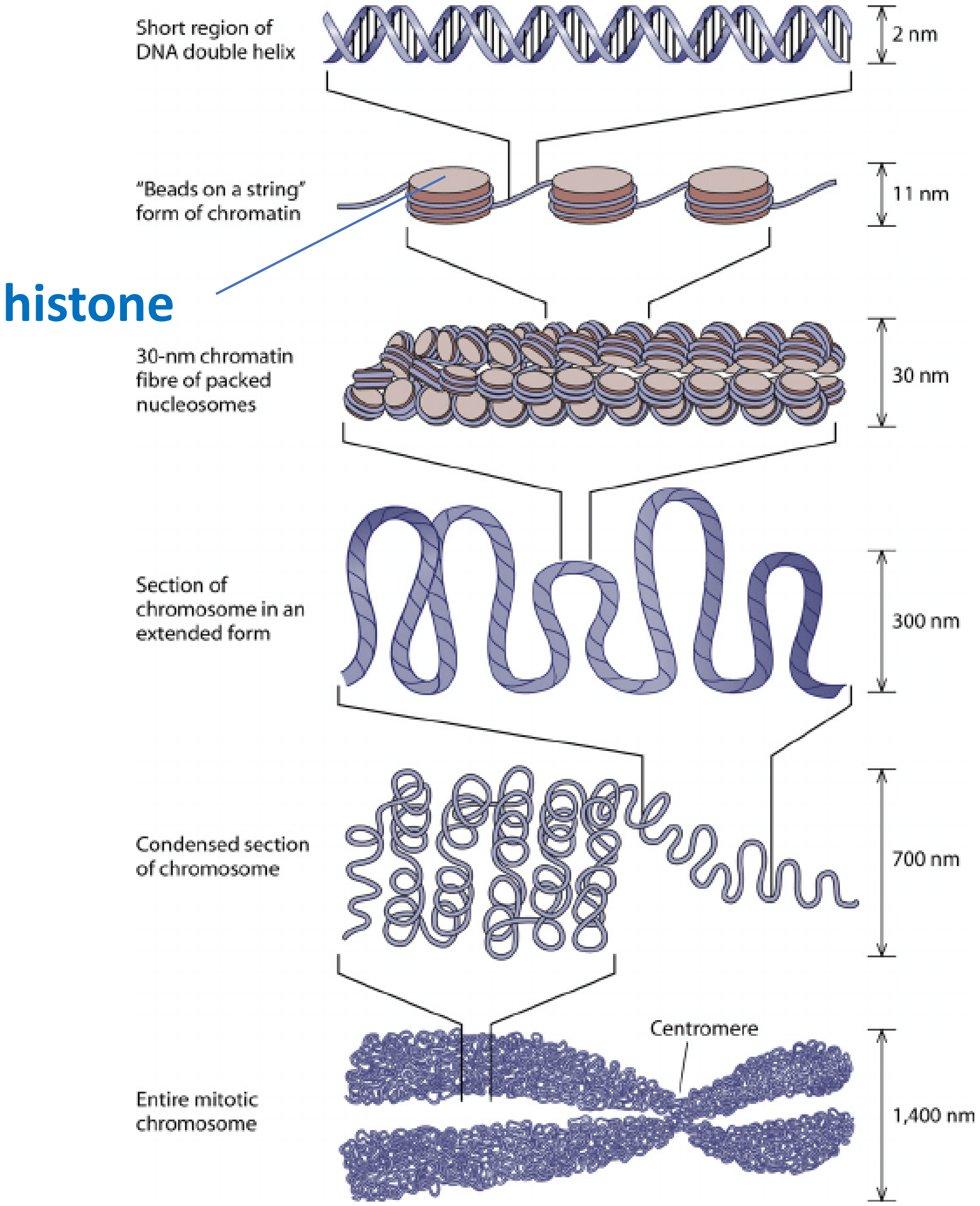


Plasma cell: many copies of *one* protein (antibody); mostly heterochromatin.



Liver cell; must make *many* proteins; little heterochromatin.

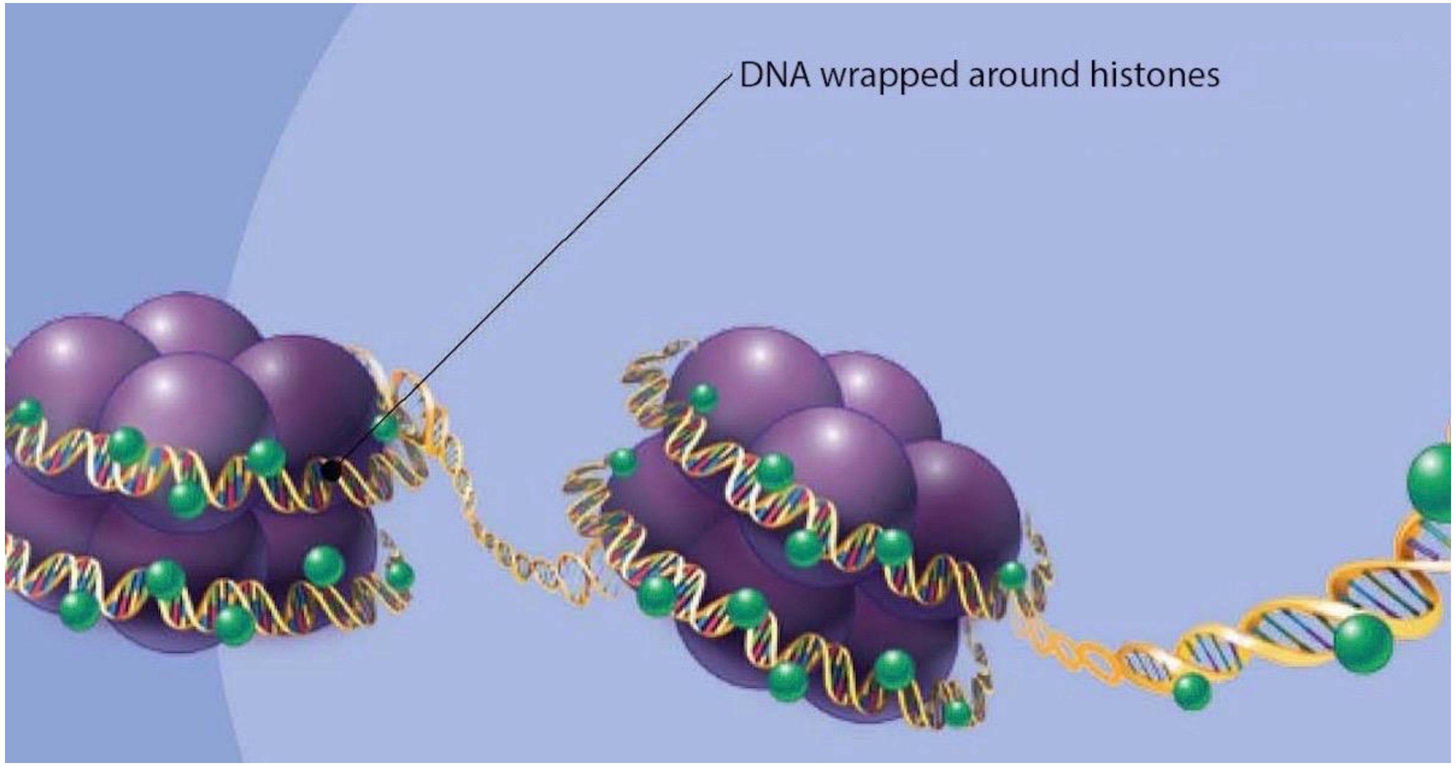
Chromatin

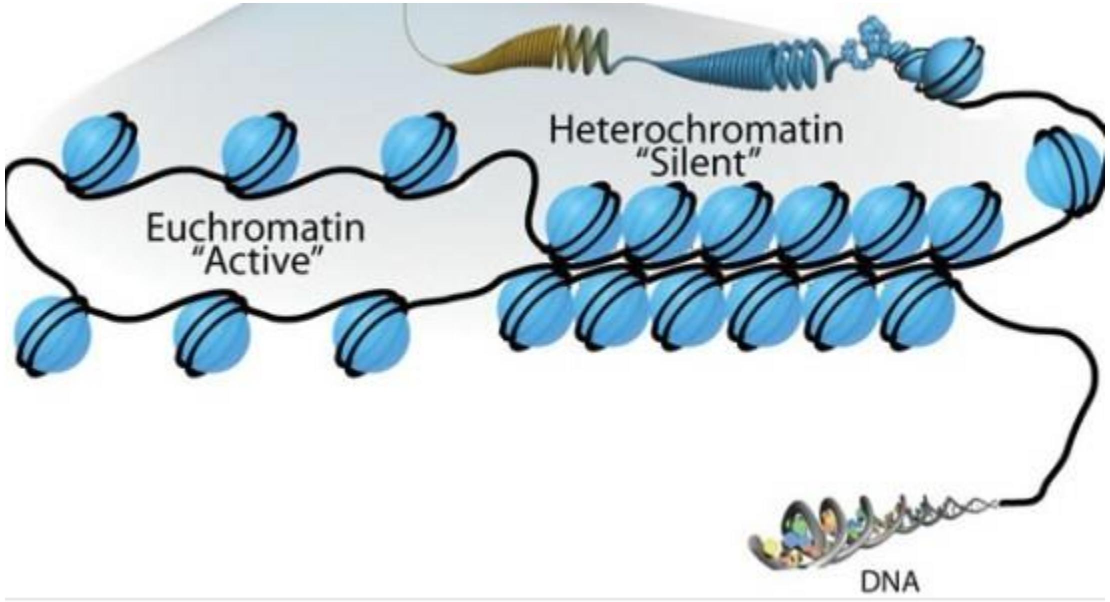


The "library" of the cell, containing all the information to make all cell components and enzymes for metabolism. Consists of **DNA and associated proteins** that organize the strands. Each of our 23 pairs of chromosomes is one long strand of DNA.

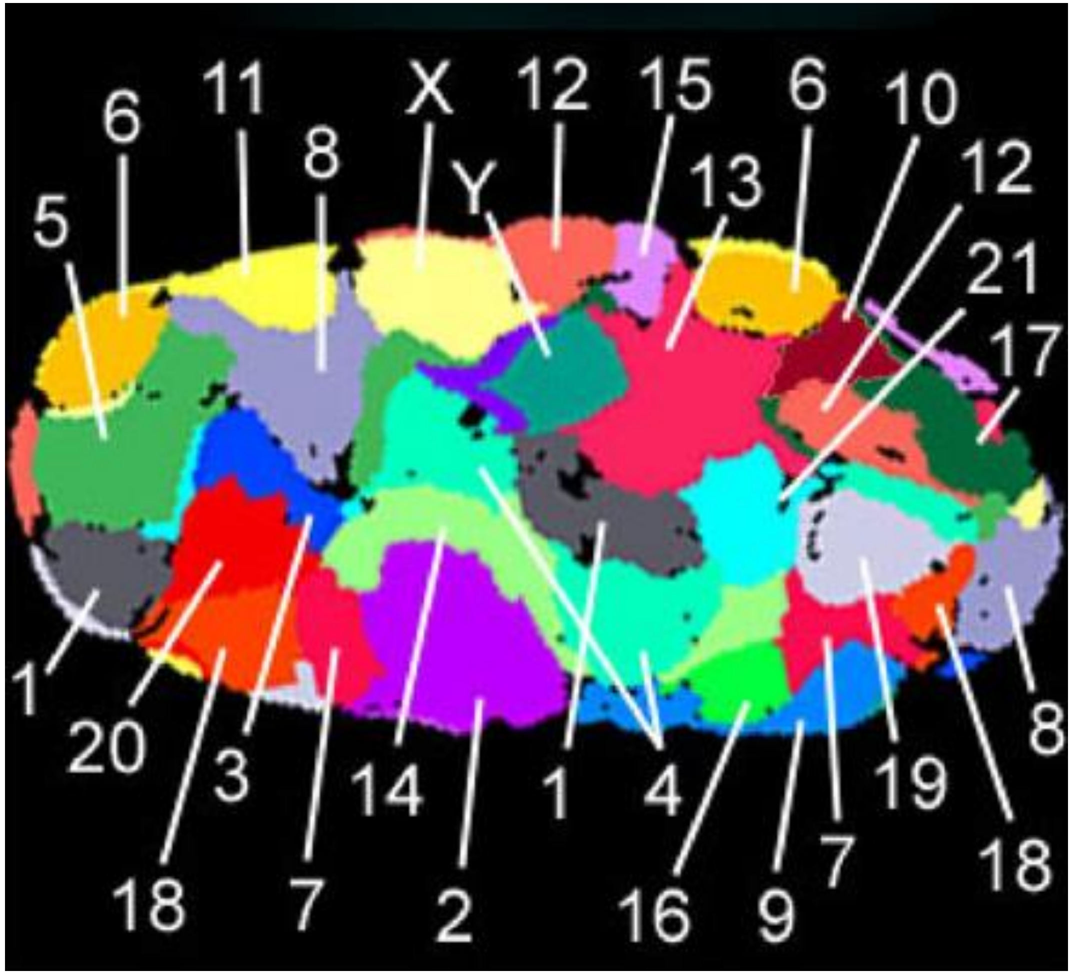
Histones

DNA is wrapped around histones, like “beads on a string”. When active, the dynamic histones allow access to make RNA. When silent, the histones pack together. Chromosomes only visible to light microscope when dividing and ultra-condensed.

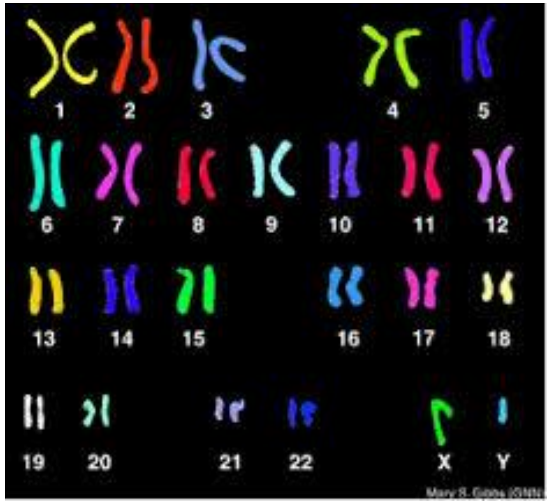




Chromosomal territories



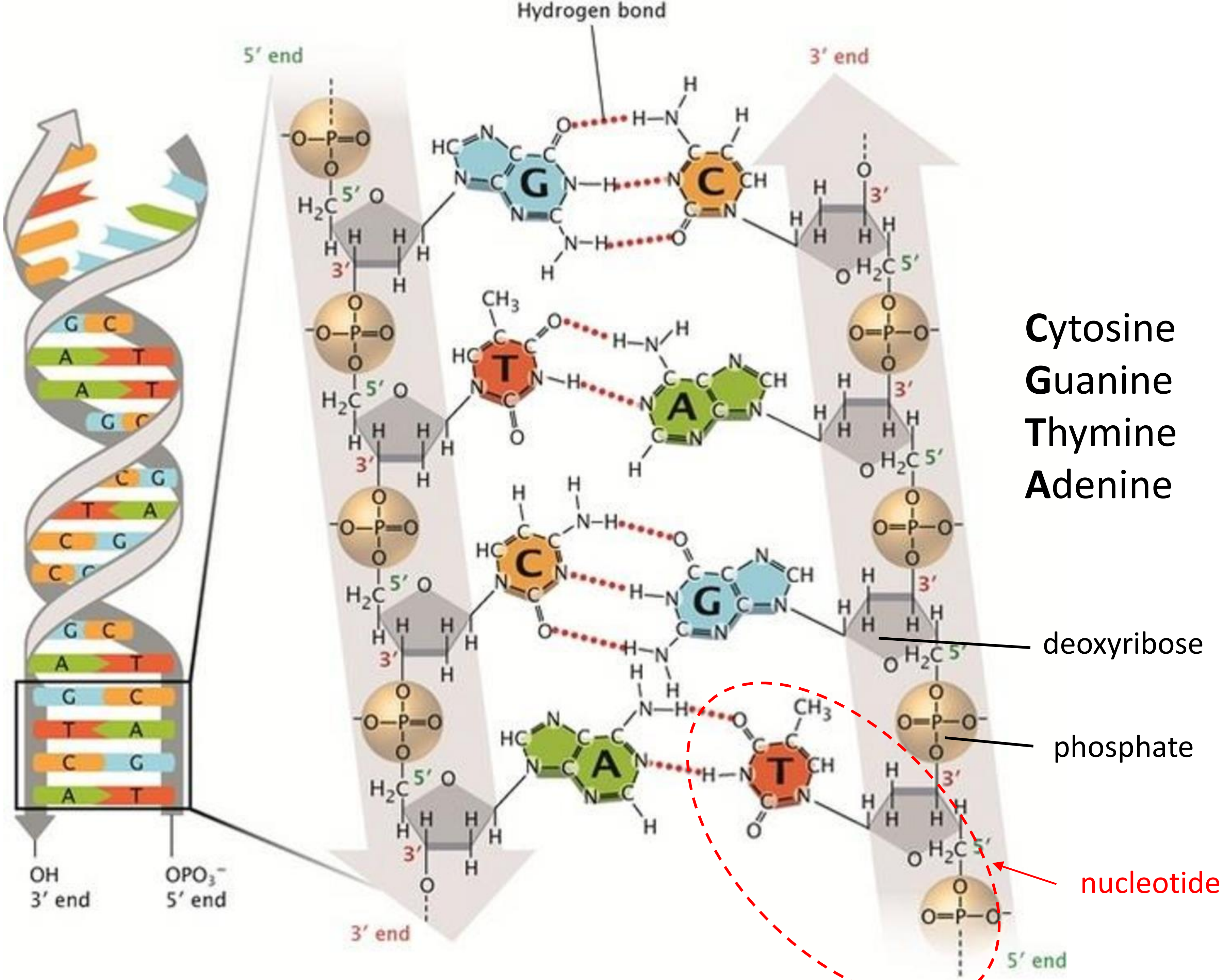
Each chromosome has its own territory within the nucleus, organized by intermediate filaments.



karyotype

DNA

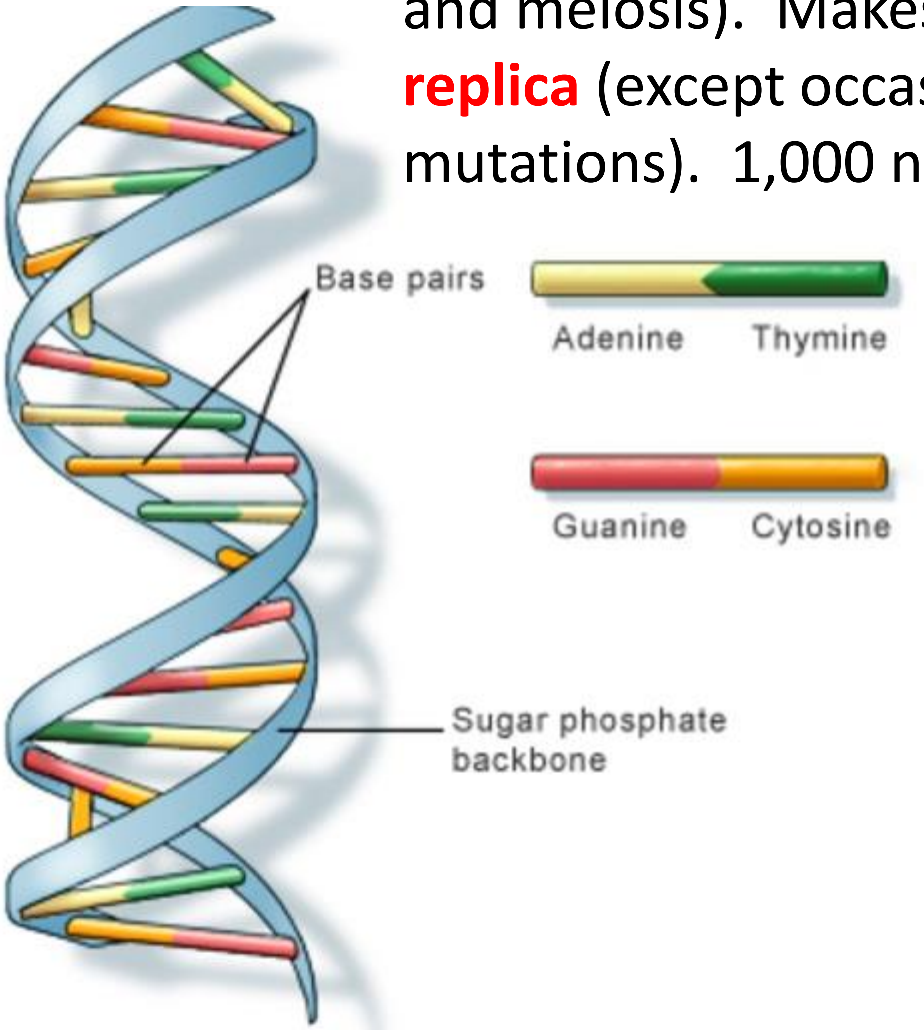
Alphabet of C, G, T and A bases.
A binds only to T, C to G. **Order of bases = information.**
Helices bound to each other by many weak hydrogen bonds.

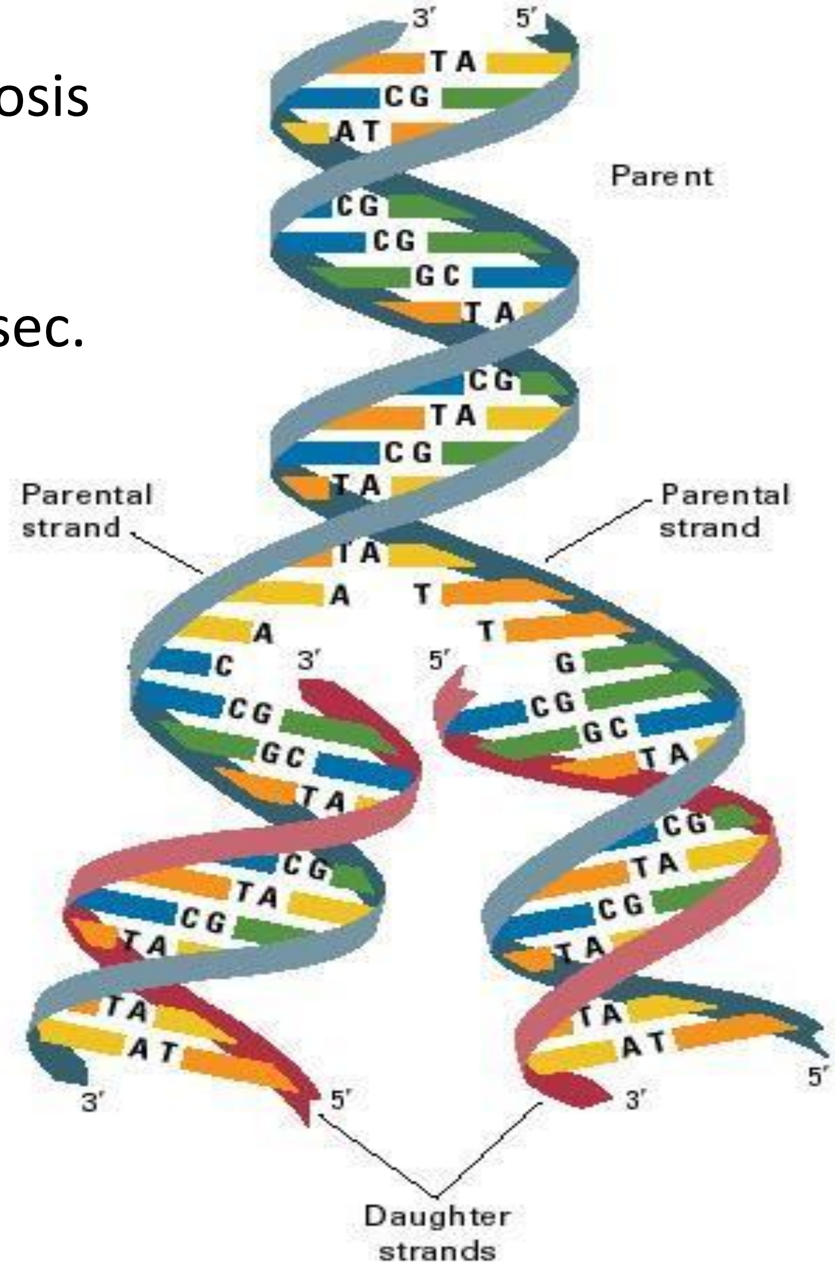


Cytosine
Guanine
Thymine
Adenine

DNA replication

Happens during cell division (mitosis and meiosis). Makes an **exact replica** (except occasional mutations). 1,000 nucleotides / sec.

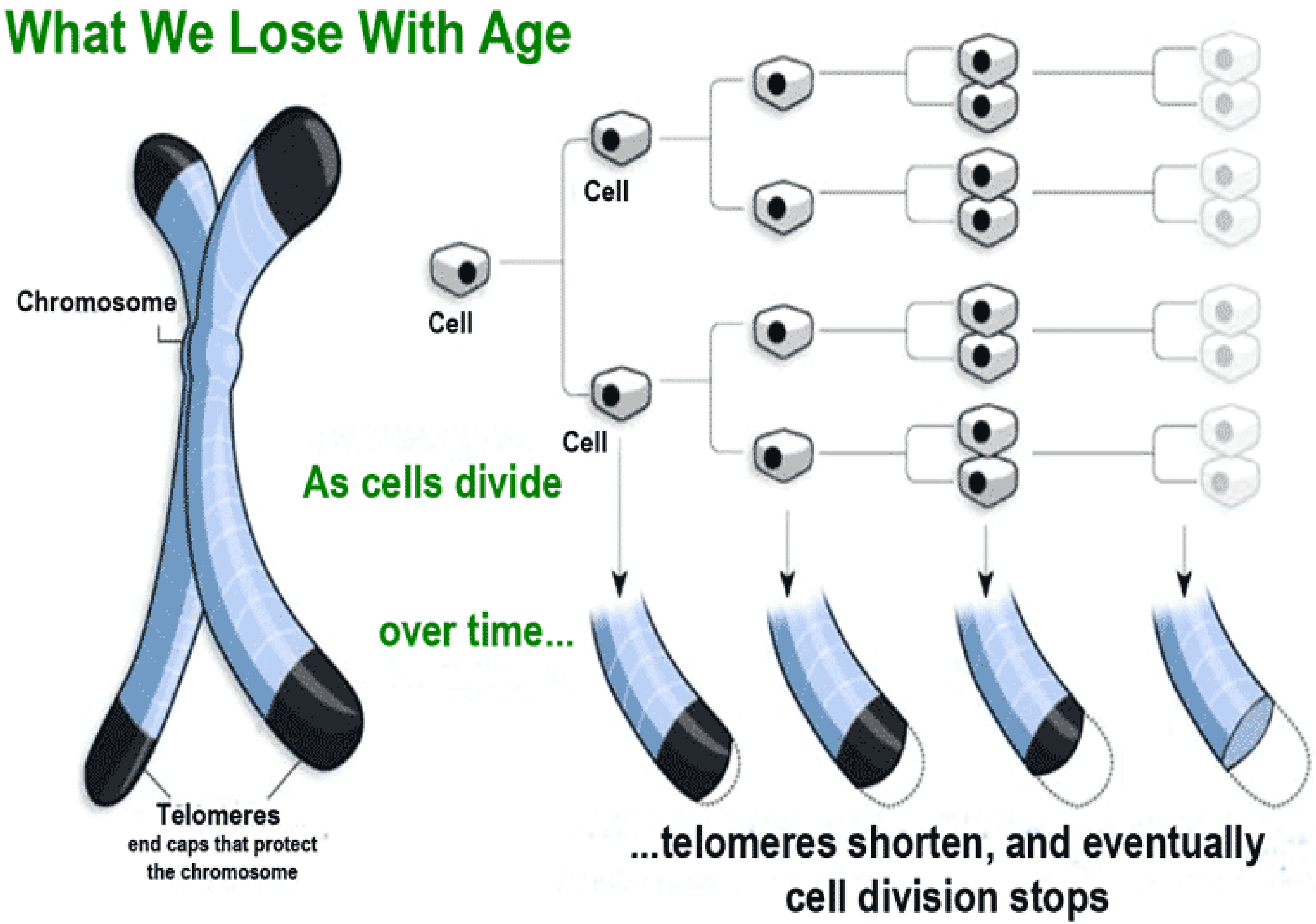




Telomeres

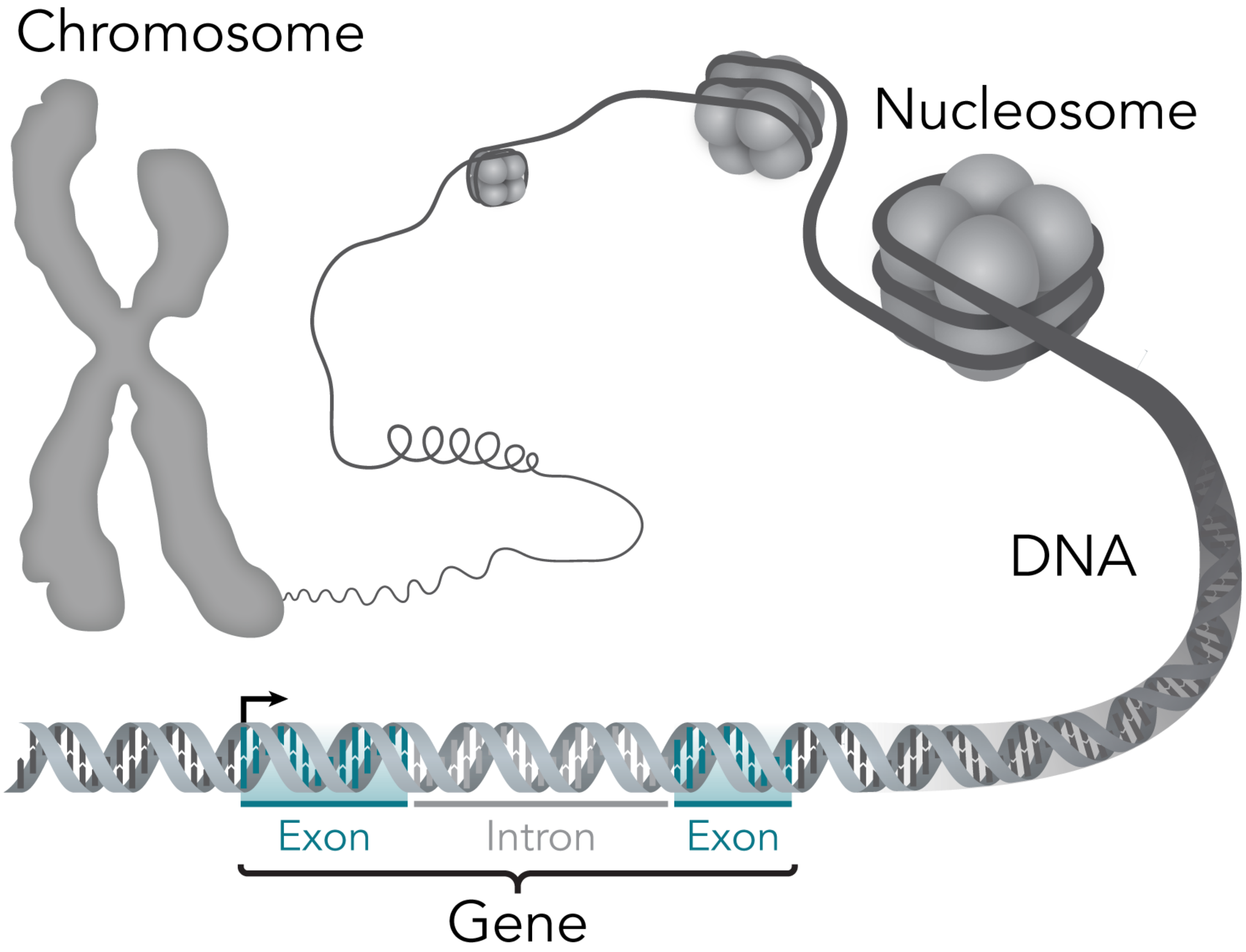
End regions of the chromosome that protect during multiple replications.

Stem cells have mechanisms to retain telomeres, so mitosis can continue indefinitely.

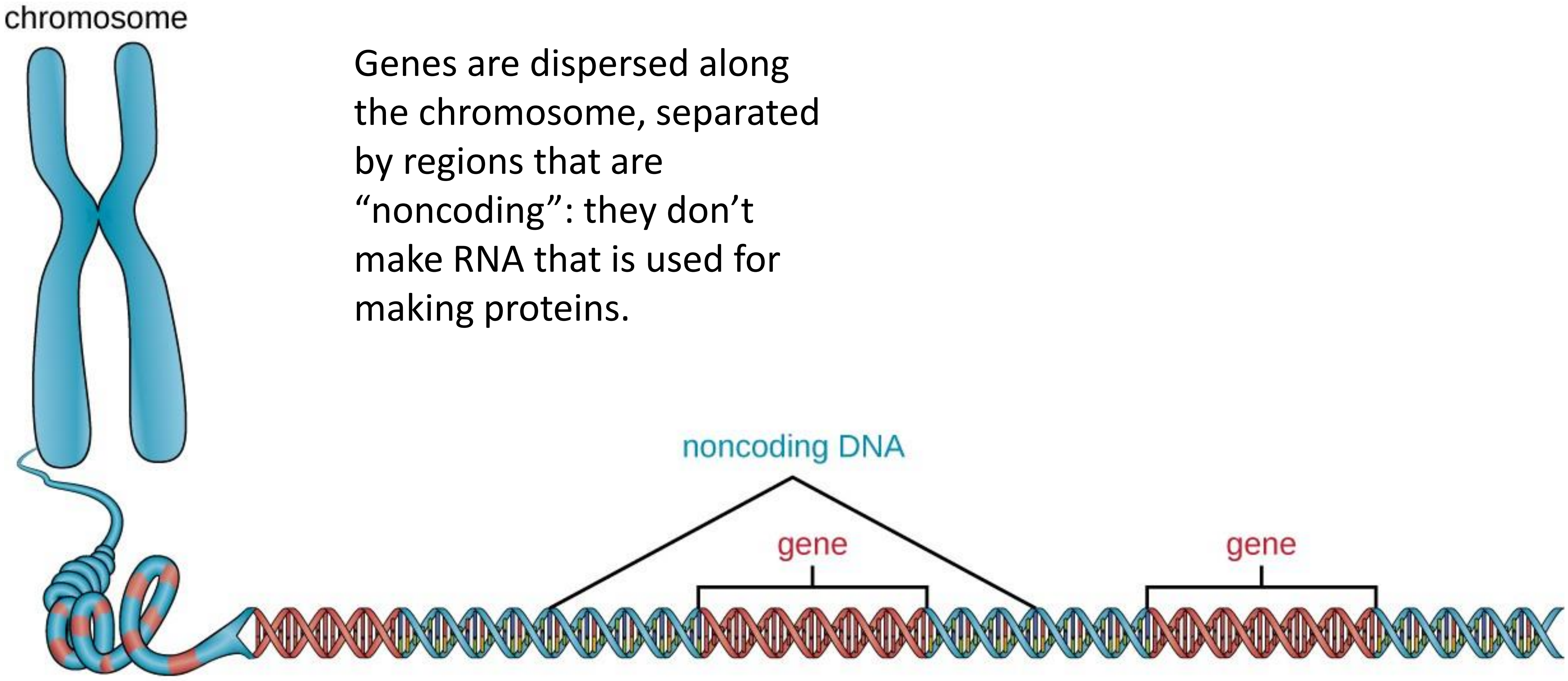


Genes

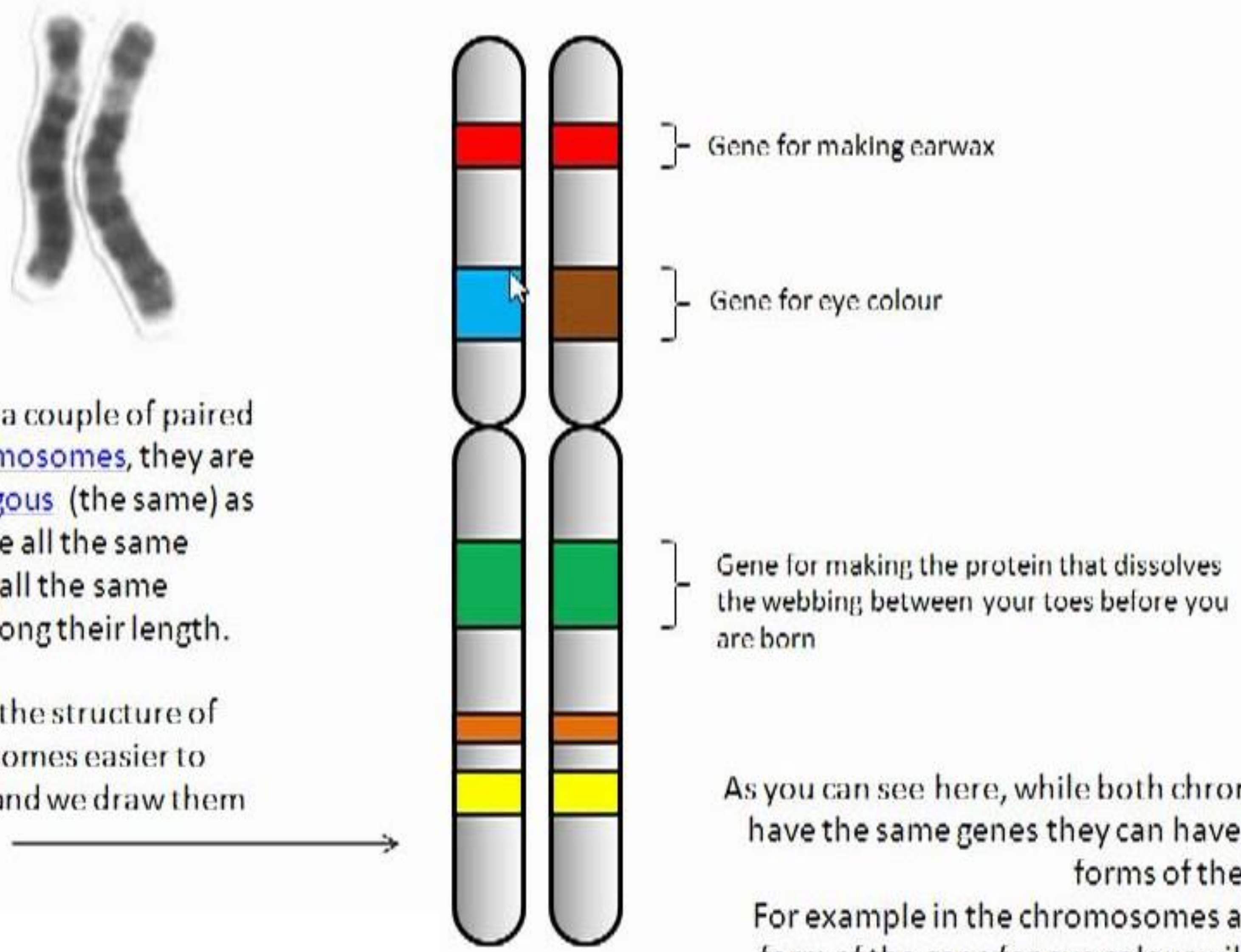
A **gene** is a segment of a chromosome that can be used to make protein. Other portions of the chromosome may produce regulatory RNA (which control gene expression) or junk?



Genes are dispersed along the chromosome, separated by regions that are "noncoding": they don't make RNA that is used for making proteins.



You have one gene for a particular protein from Mom and one from Dad; they may be **alleles** of the same gene.

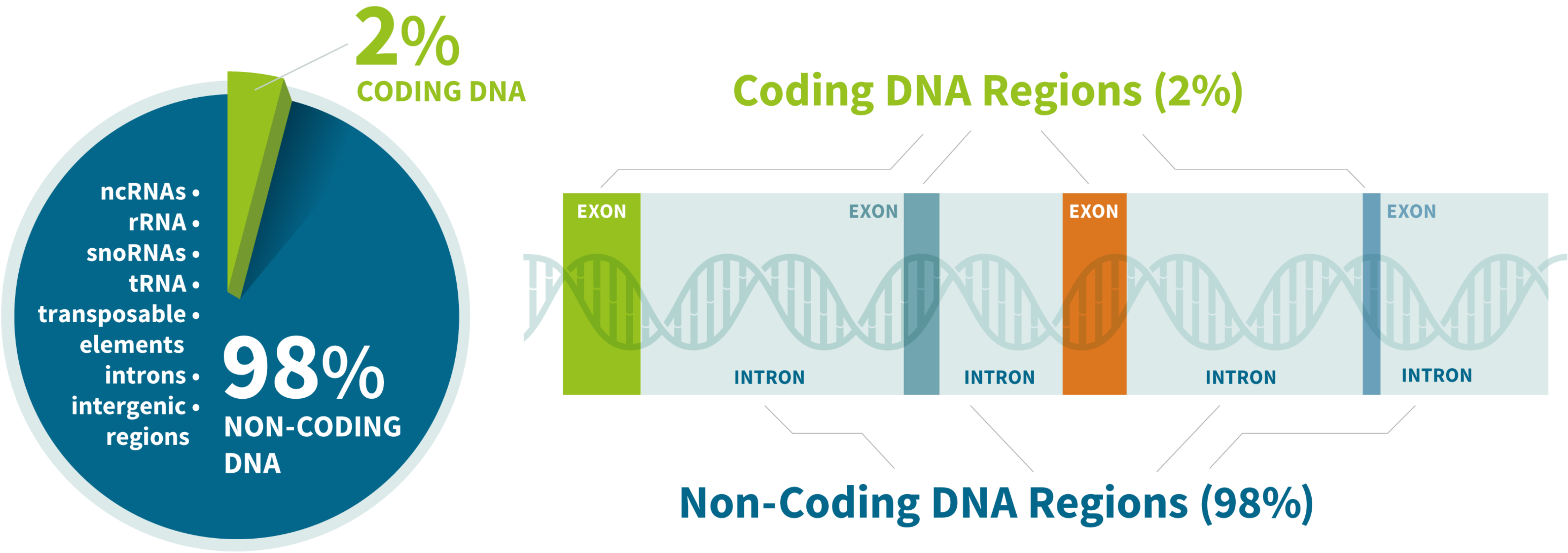


Above is a couple of paired up Chromosomes, they are homologous (the same) as they have all the same genes in all the same places along their length.

To make the structure of chromosomes easier to understand we draw them like this

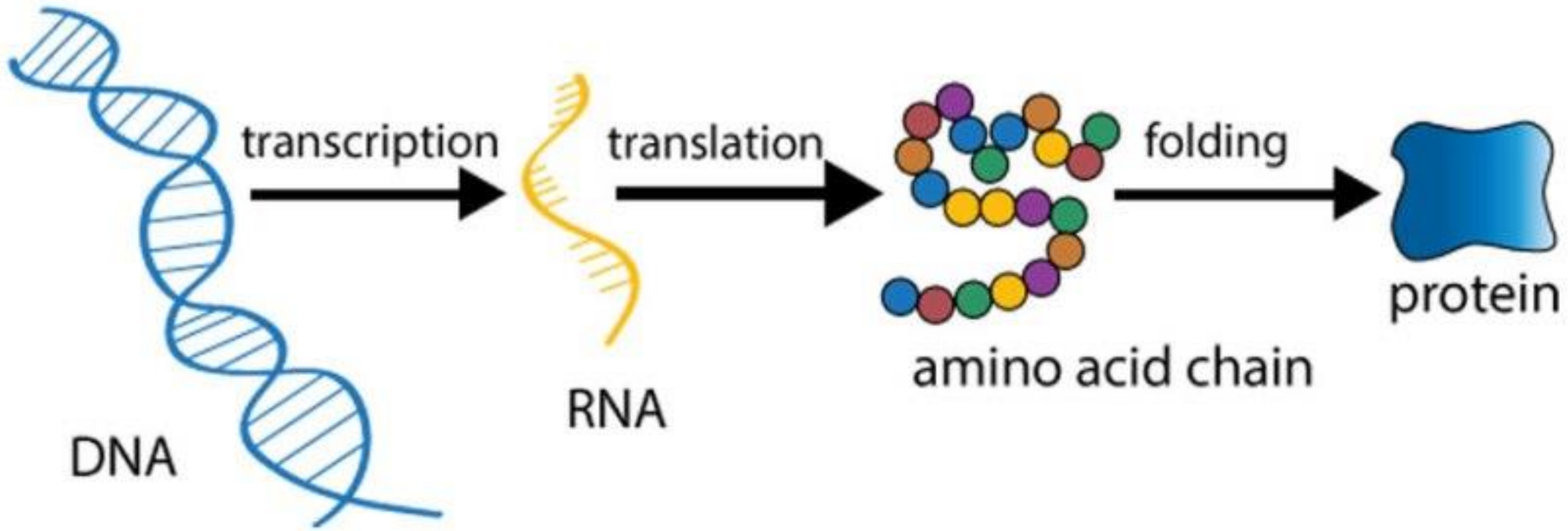
As you can see here, while both chromosomes have the same genes they can have different forms of these genes.
For example in the chromosomes above one form of the gene for eye colour will give you blue eyes and the other form will give you brown eyes.
When we have these different forms for the same gene we call these forms **alleles.**

Most of the DNA we have doesn't code for proteins. Is it all "junk"? Some codes for regulatory RNA. 8% comes from ancient viruses that got pasted in. Maybe we just don't know what the rest does.



Transcription to RNA

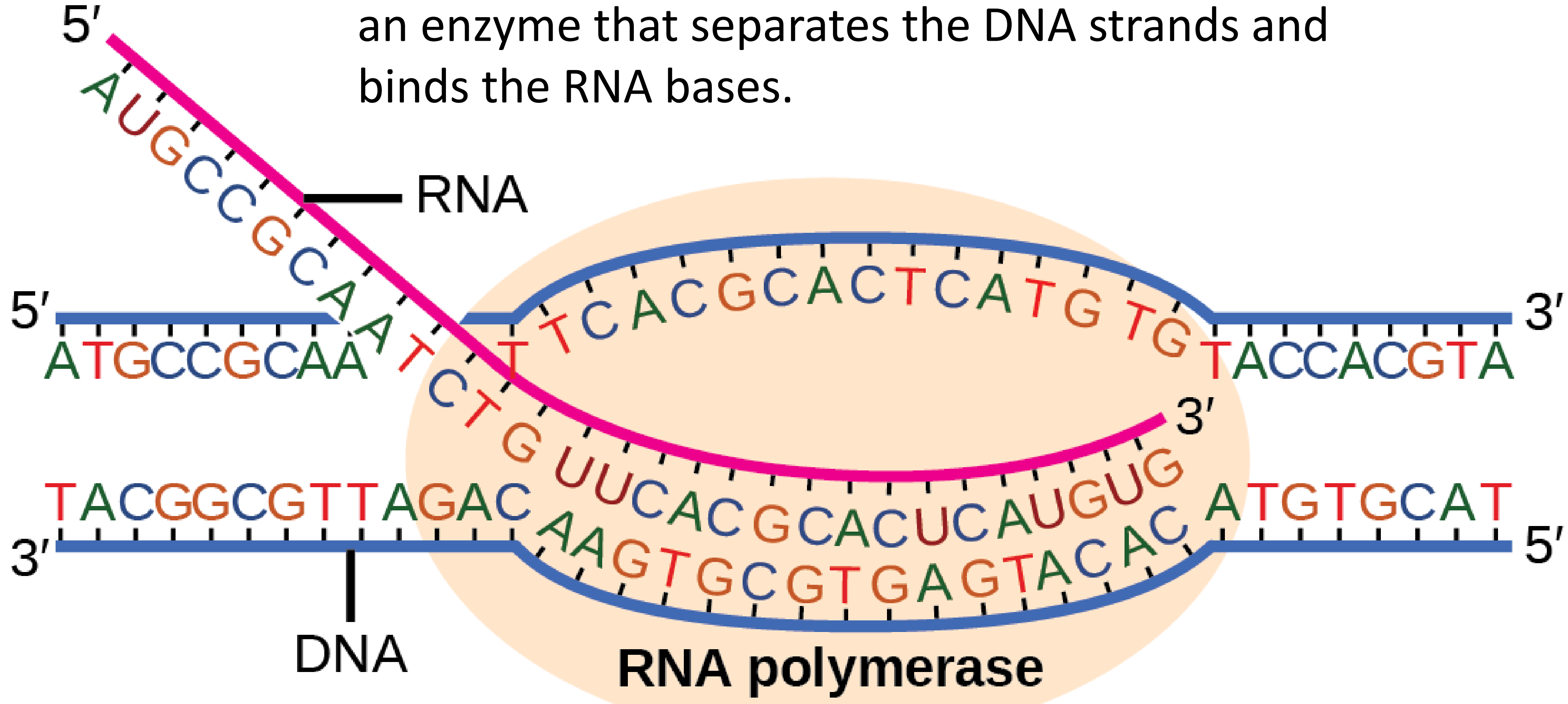
"Central Dogma"



Occurs in nucleus;
messenger RNA leaves the nucleus to be *translated into protein* in the cytoplasm.

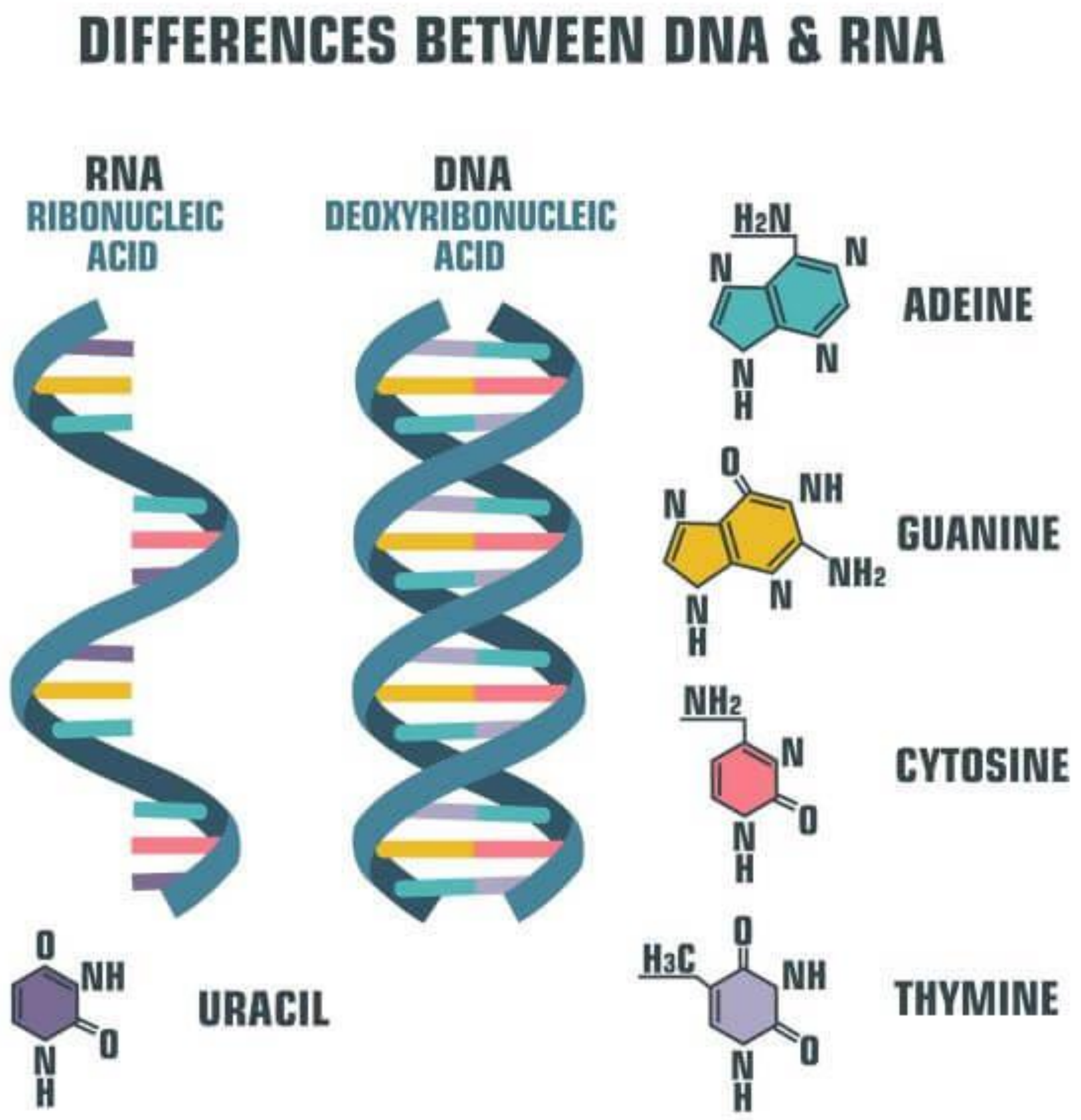
DNA Transcription to RNA

DNA can be ***replicated*** to duplicate DNA or be ***transcribed*** to make **RNA**. RNA polymerase is an enzyme that separates the DNA strands and binds the RNA bases.



RNA

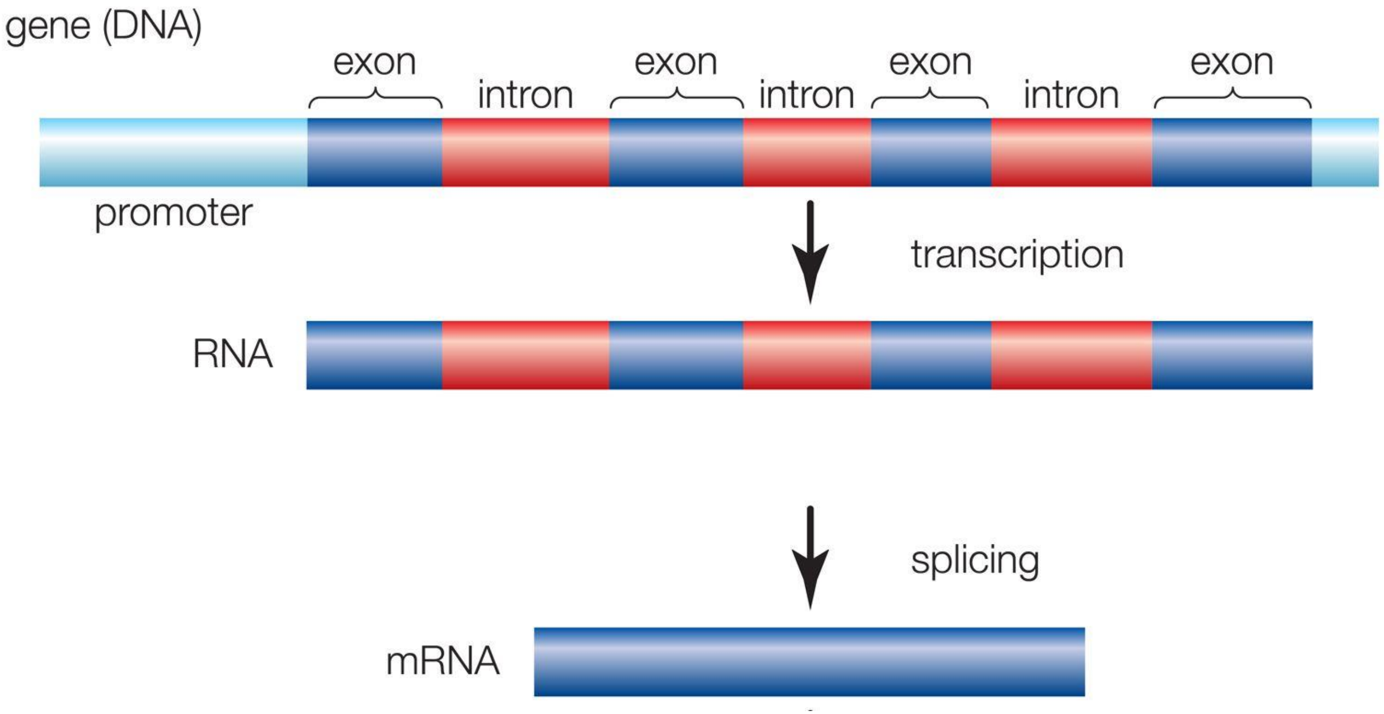
RNA has a different sugar (ribose) and one different base (uracil instead of thymine).
RNA can pass out of the nucleus to the cytoplasm, conveying the coded instructions to make proteins.
When DNA makes RNA, that gene is being **expressed**.
Must be in euchromatin form.



RNA differs by sugar, and by one base

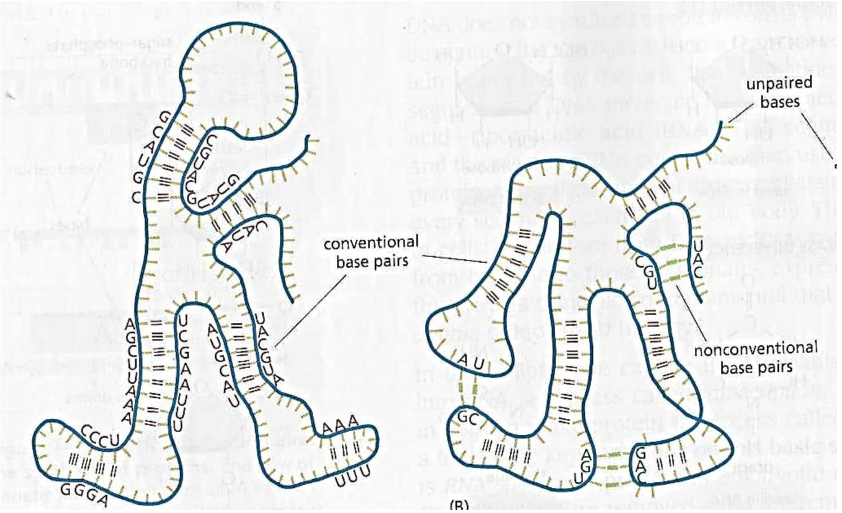
DNA and genes

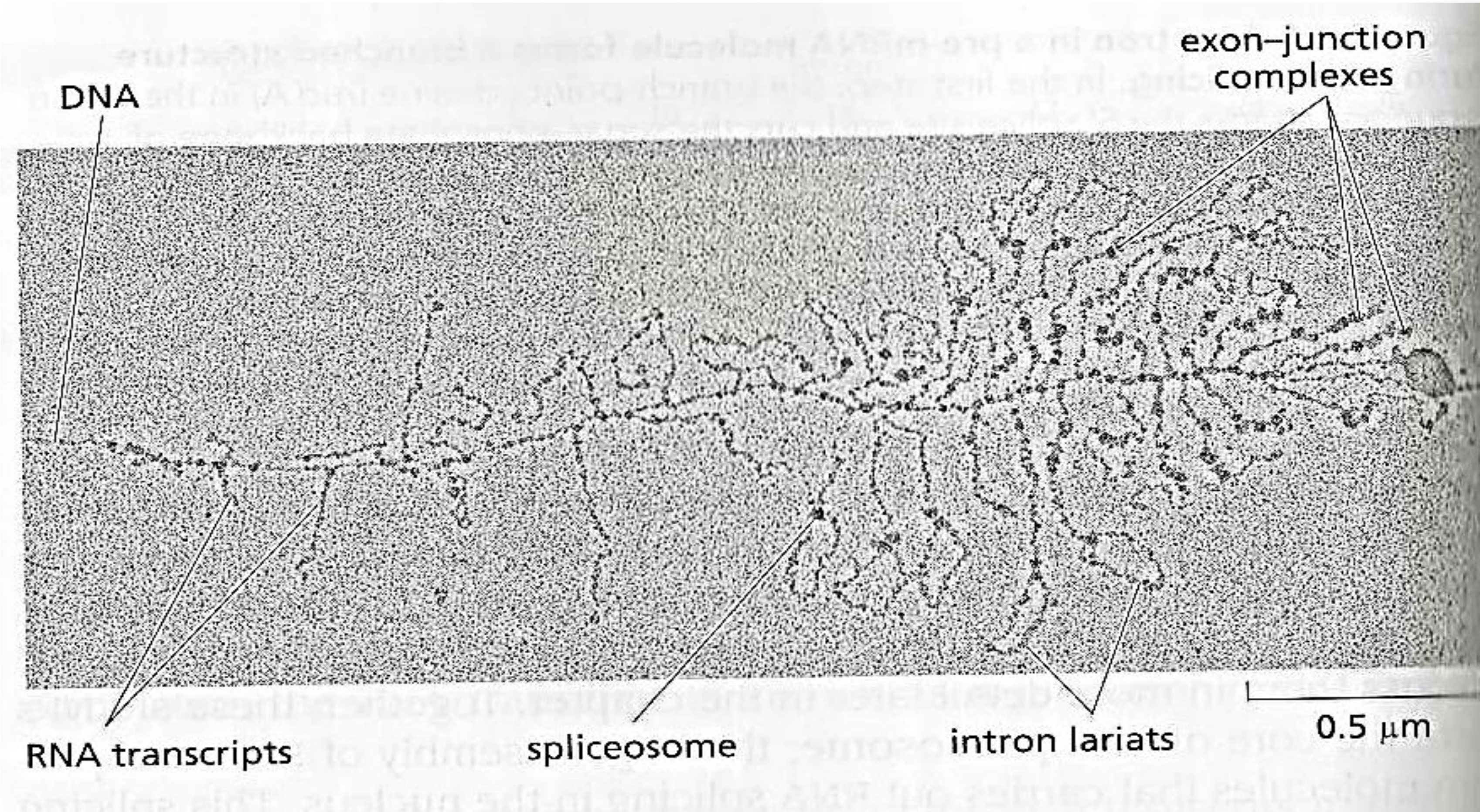
Genes are the portions of DNA that code for *particular proteins* (most DNA is non-coding for protein but may make regulatory RNA, or be left-over viral DNA, or junk). Most genes have **promotors** and inhibitors to turn them on or off. The gene includes **introns** (that get chopped out) and **exons** that get incorporated into messenger RNA. The exons can be mixed in various combinations (**spliced**) to produce different mRNAs (messenger RNA).



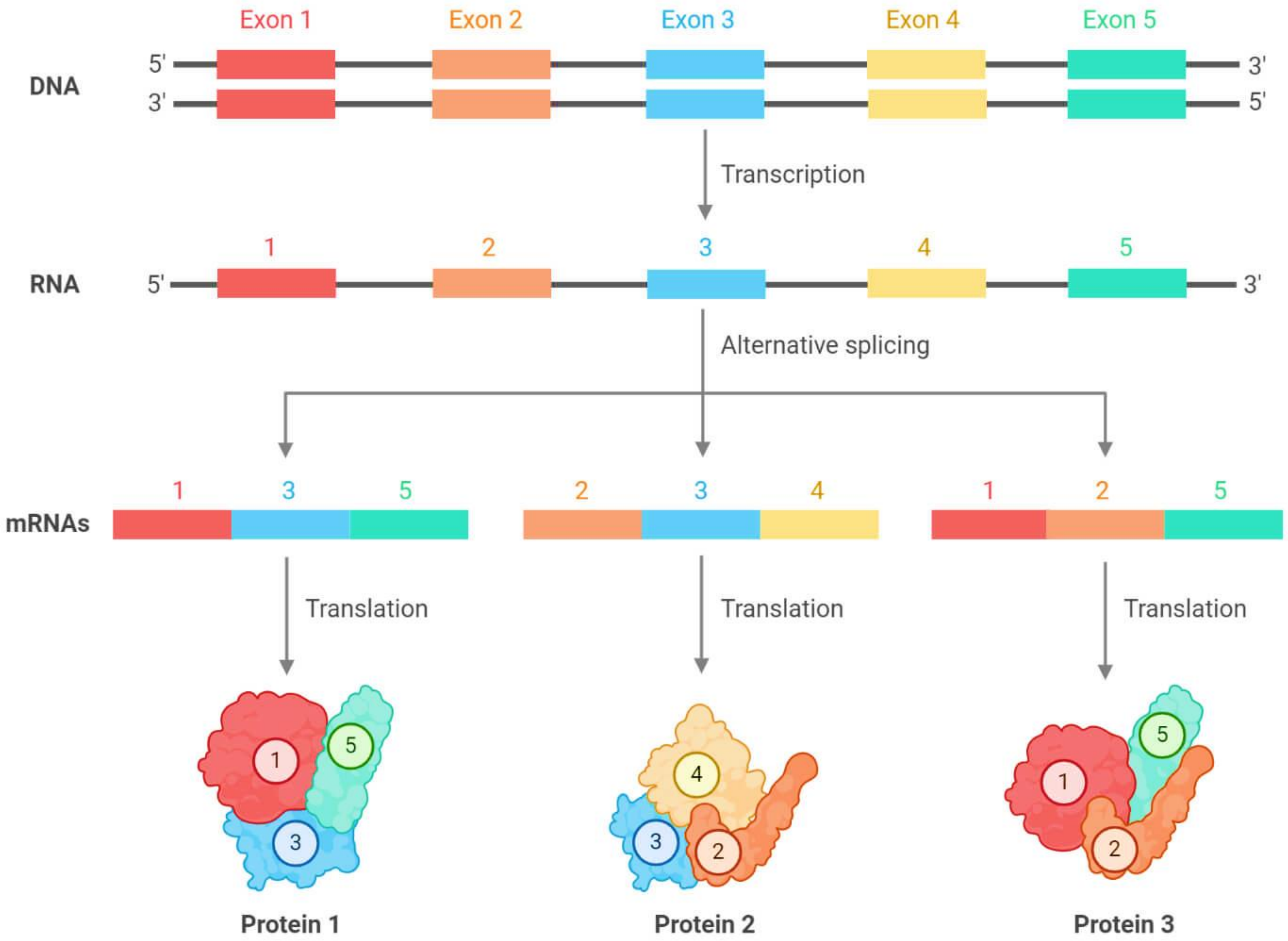
RNA Splicing

Unlike DNA (double helix), RNA can take many shapes, acting in structural, regulatory or catalytic roles.
EG: Splicing is done by **Snurps** (small nuclear ribonucleoproteins) that are at the core of a **spliceosome**.



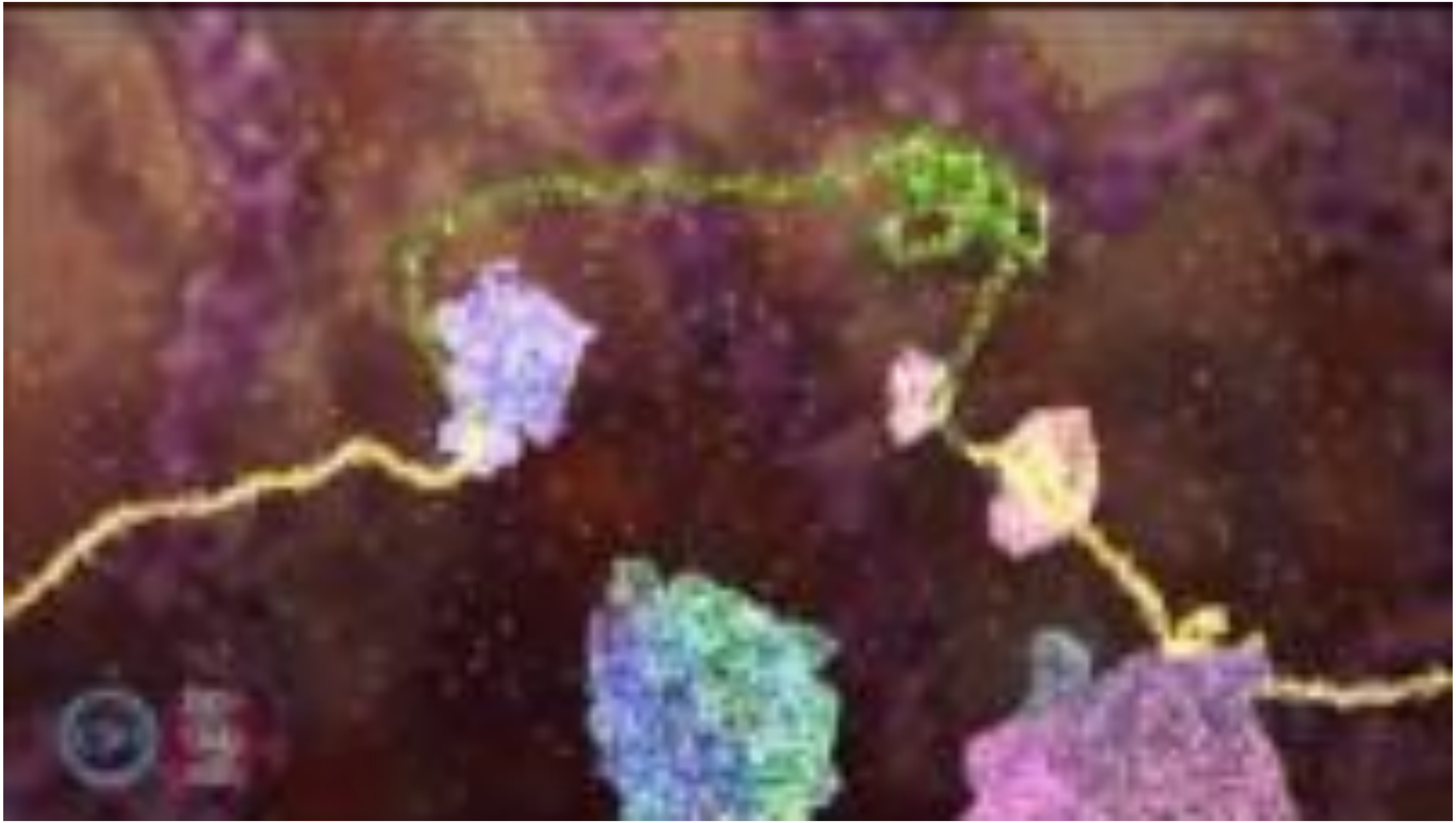


Alternative splicing



Many different proteins can be made from one gene!

Splicing

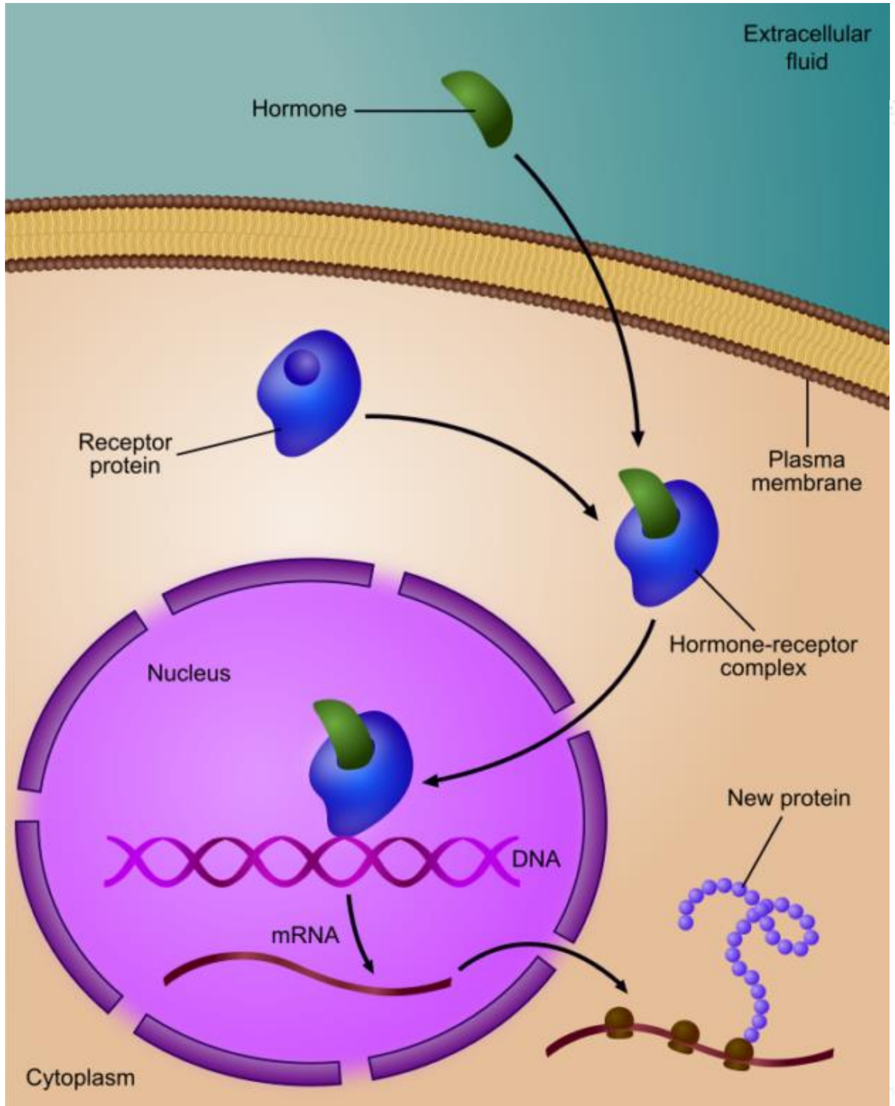


Gene Expression

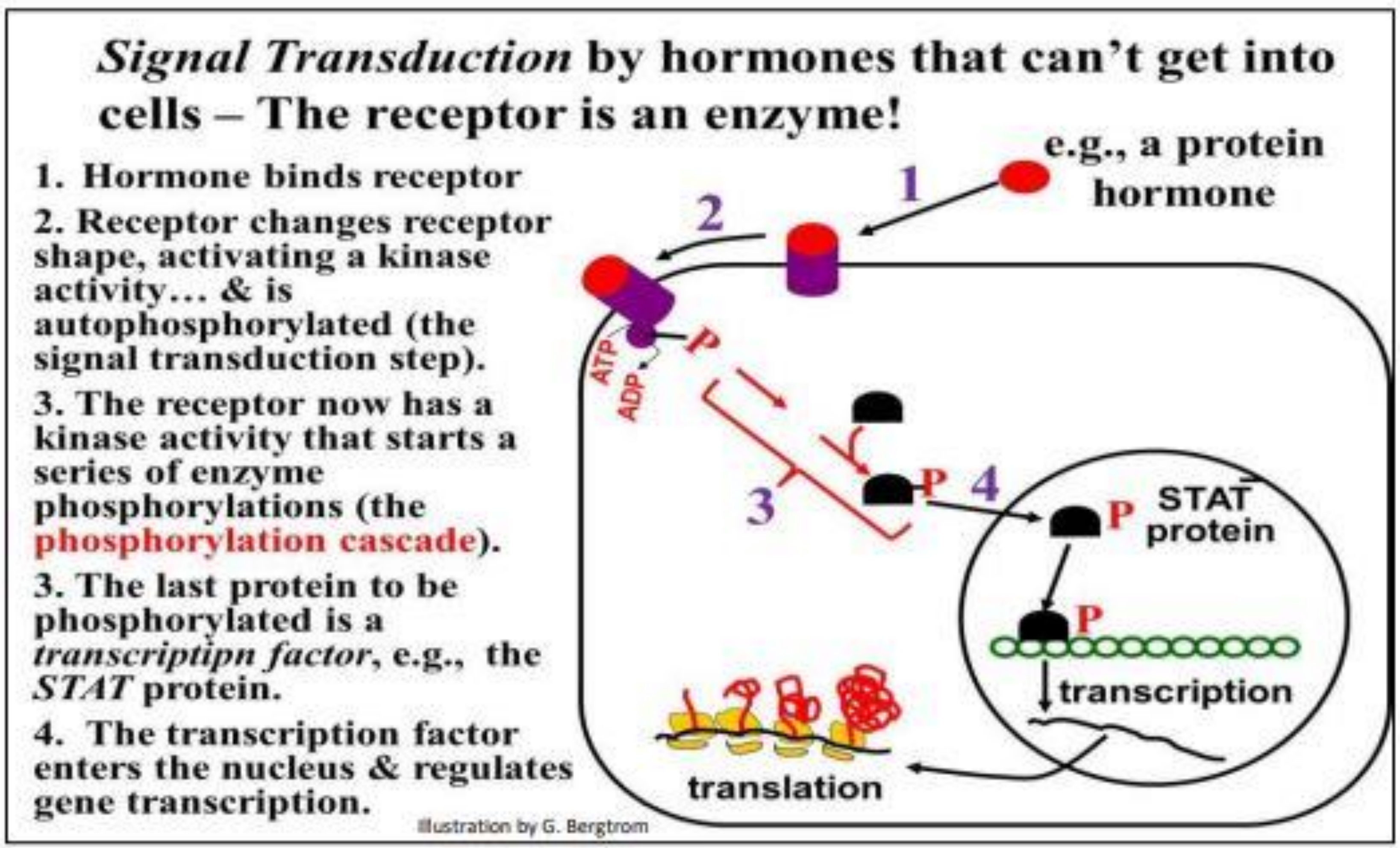
Cell carefully regulates gene expression, in place and time. Different cell types activate different genes.
Genes are regulated by *transcription factors*, which may be controlled by hormones, regulatory RNAs, growth factors, morphogens, other signals from surrounding cells or matrix. Signals may be chemical, mechanical or electrical; they work by altering gene expression. The transcription factors attach to the promotor regions and start the transcription of the DNA.

Gene Regulation by hormones

Steroid hormone



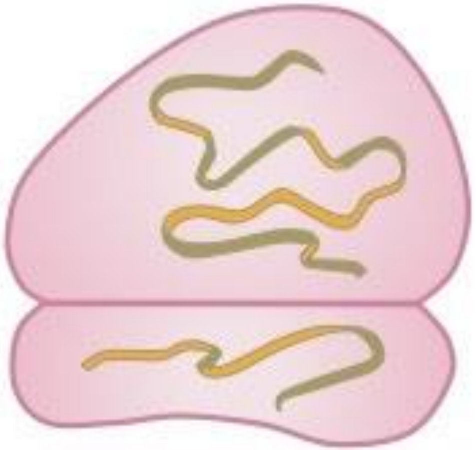
Protein hormone



3 kinds of RNA

Messenger RNA contains the instructions for making proteins.
Ribosomal RNA makes the **ribosomes**, the factories in the cytoplasm where proteins are created.
Transfer RNA reads the code of the mRNA and ferries the protein building blocks (amino acids) to the ribosome.
Ribosomal RNA transcribed and processed in the ***nucleolus*** of the nucleus.

Messenger RNA (mRNA)

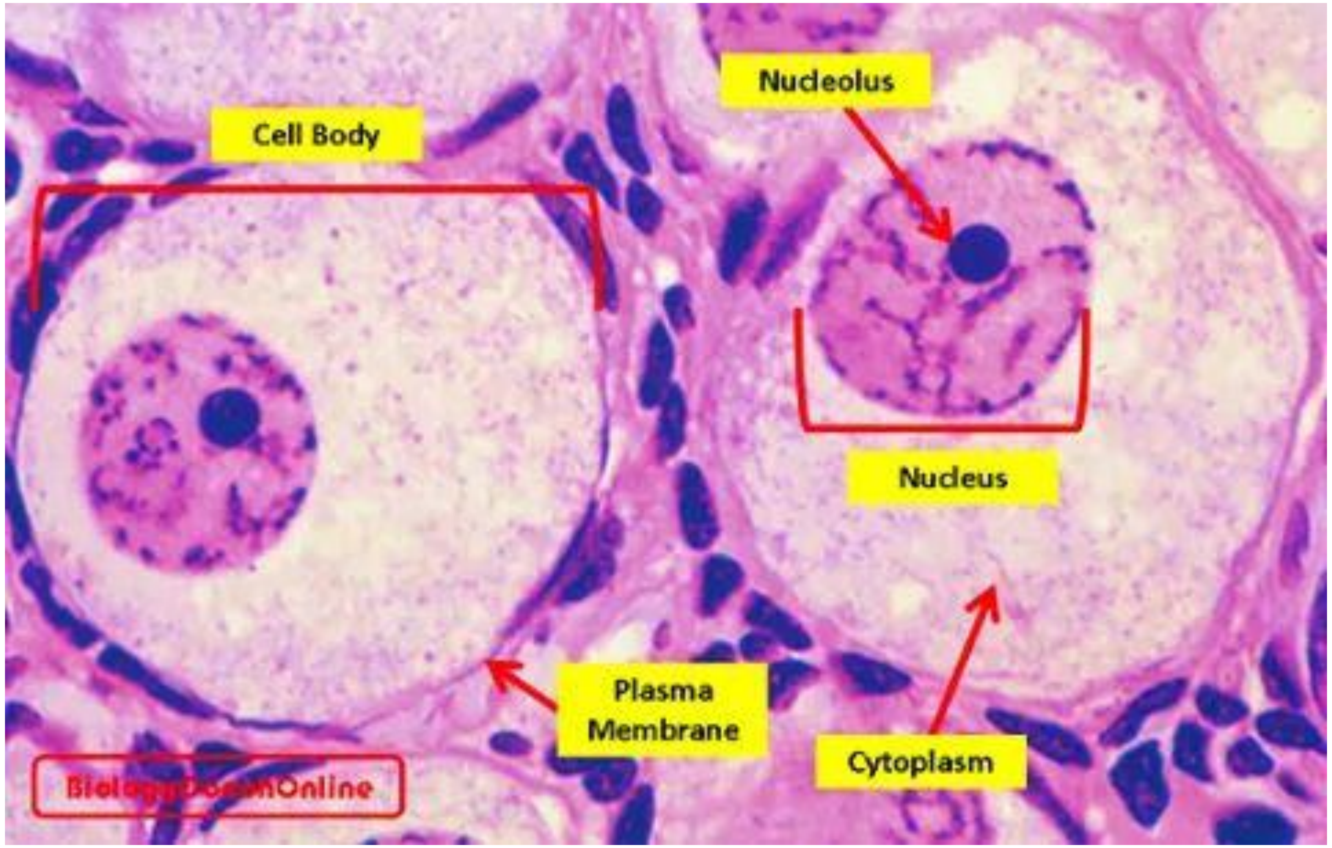


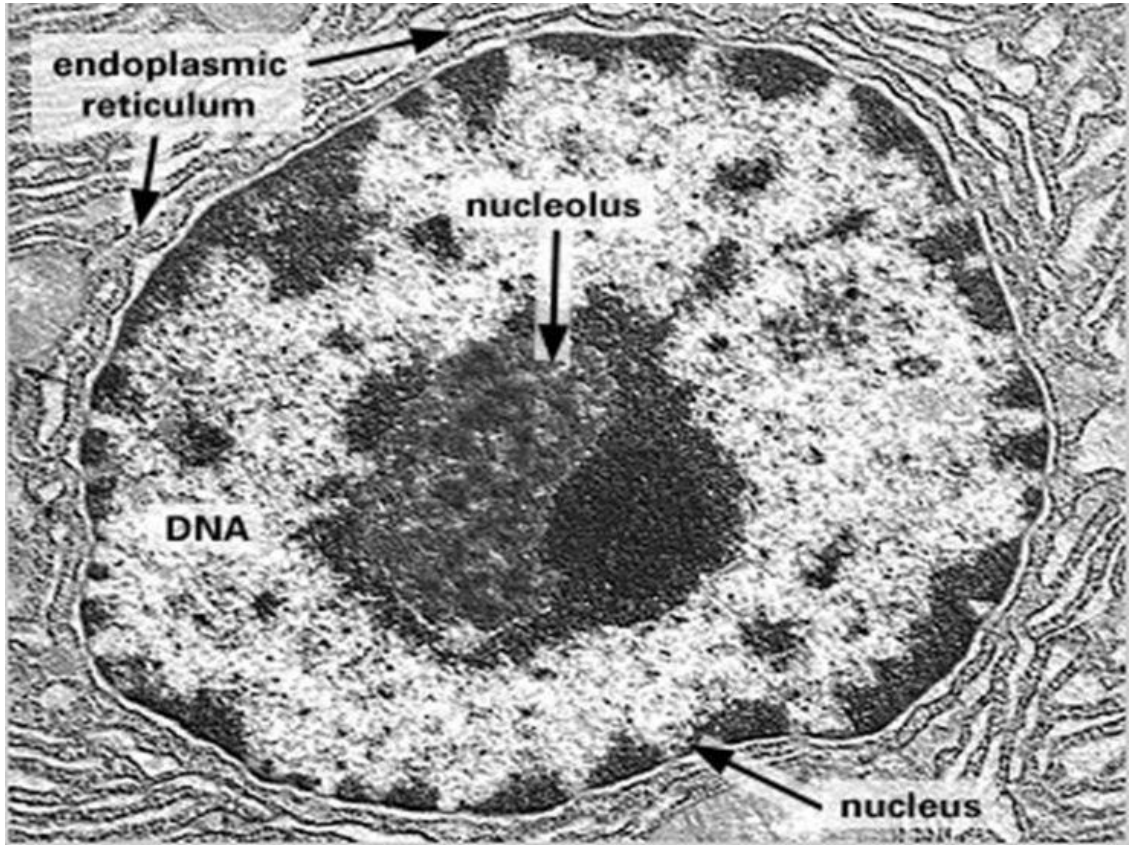
Ribosomal RNA (rRNA)

Transfer RNA (tRNA)

Nucleolus

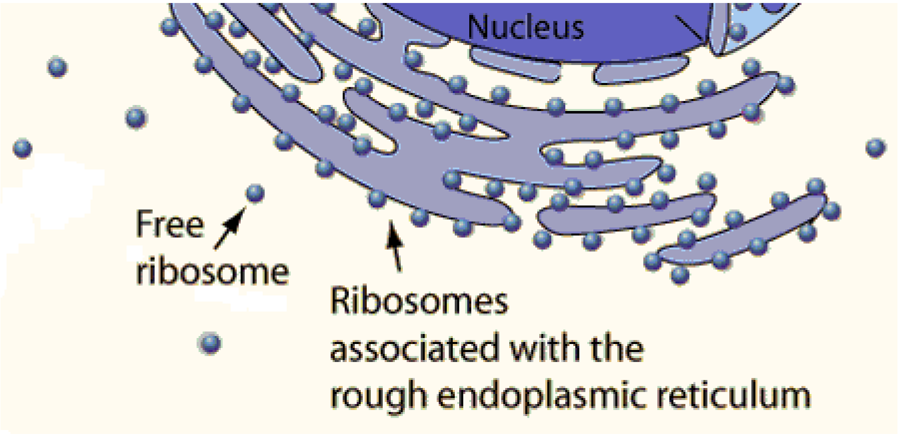
Ribosomal RNA is concentrated and assembled with proteins into ribosome subunits within the **nucleolus**, then transported out of the nucleus.

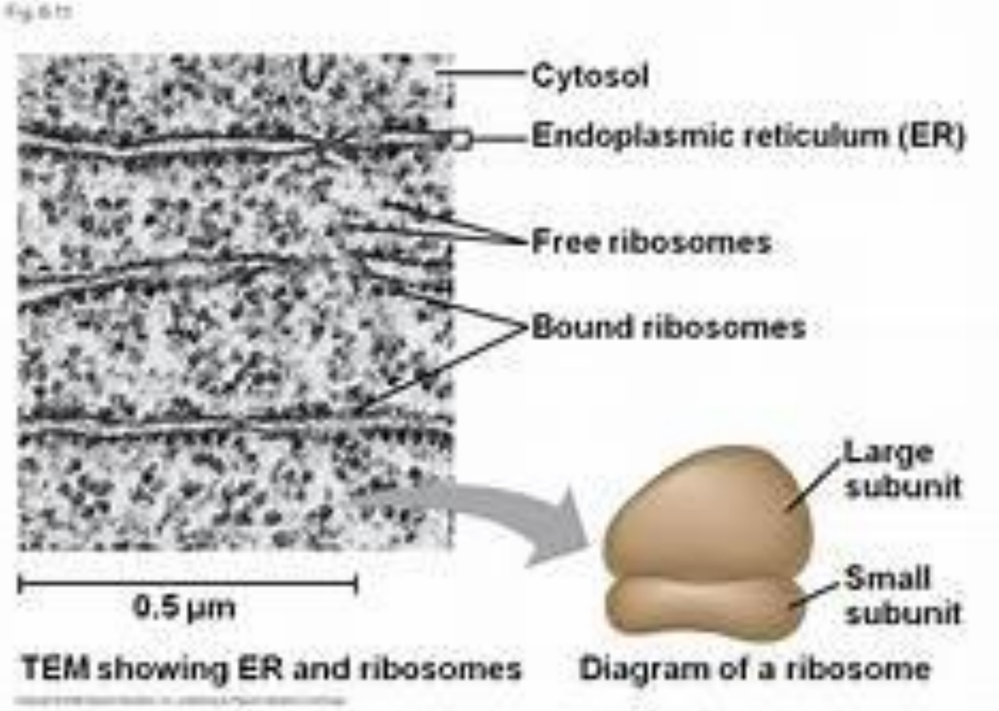




Ribosomes

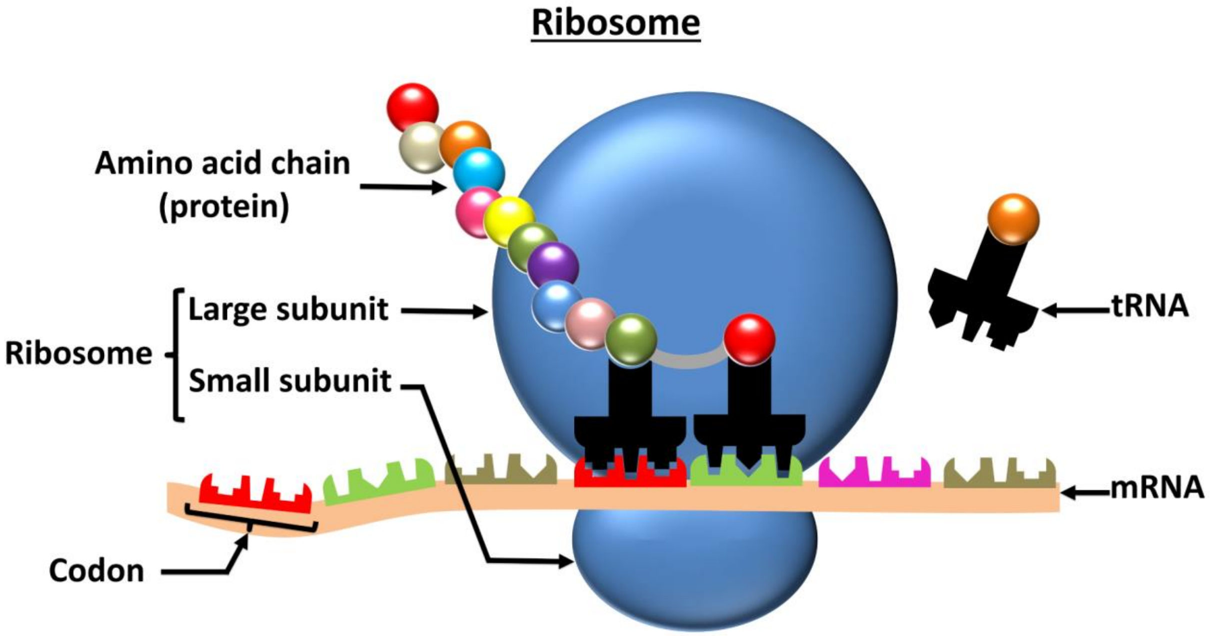
Final assembly of ribosomes is done in the cytoplasm. **Free ribosomes** make proteins for the cell cytoplasm; ribosomes attached to the endoplasmic reticulum make proteins for export or cell organelles.





TEM showing ER and ribosomes

Diagram of a ribosome



DNA : Cell Structure and function

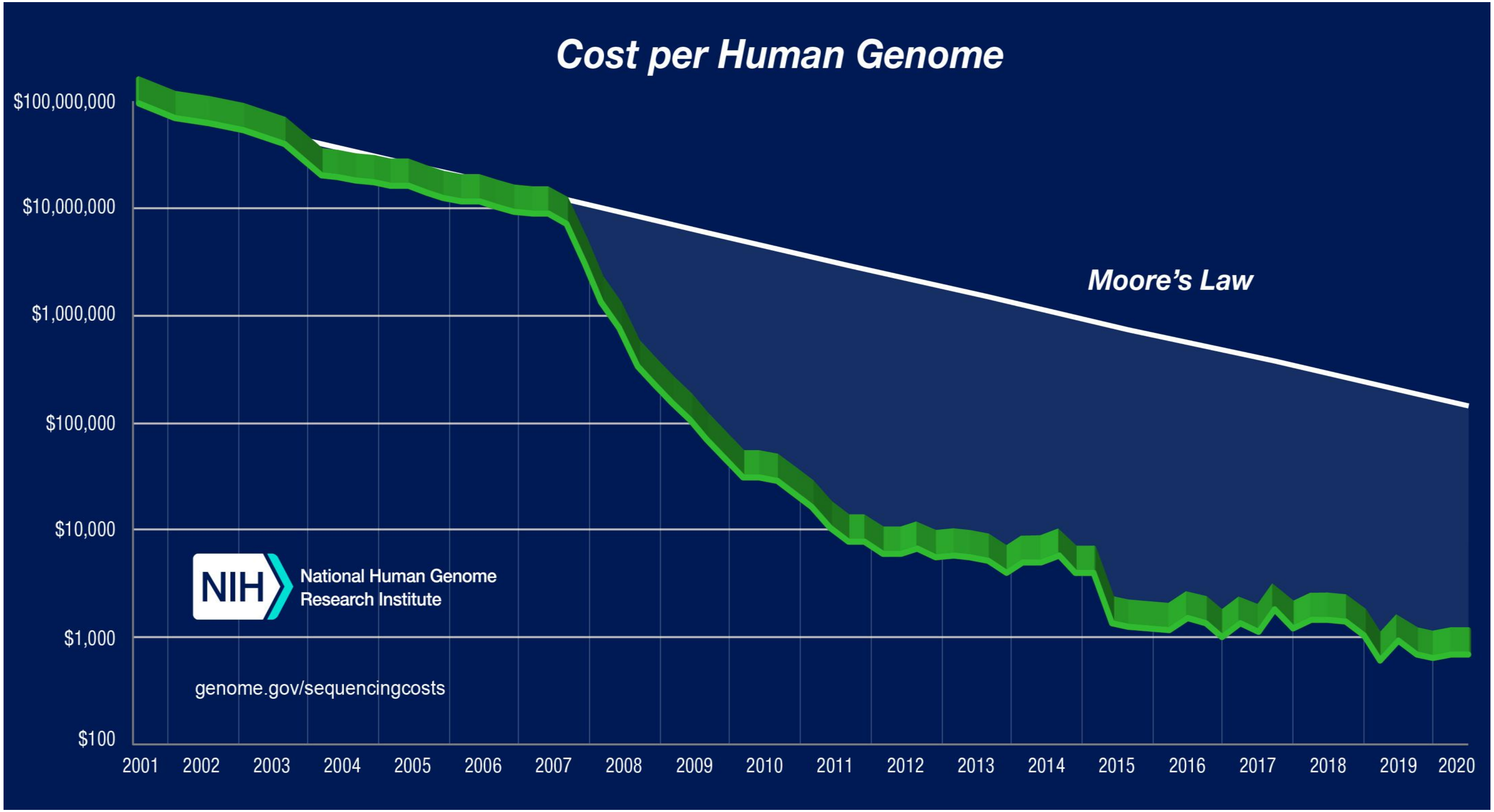
DNA has **direct** control over the synthesis of structural proteins of the cell. DNA has **indirect** control over metabolism by synthesizing enzymes that control each step of metabolism. All cells in the body have the same DNA, but different cell types express different genes. How do cells specialize?

Which genes on the DNA are active? *Promoters* turn the genes on (transcription), while *inhibitors* turn them off. *Transcription factors* activate the promoters or inhibitors. (Also epigenetic markers can suppress expression.)

Changes in the cytoplasm or signals from outside the cell (hormones, metabolites, substrate, etc) cause expression or inhibition of particular genes. So which genes are expressed will be different for each cell type, changing during development, in response to changing signals.

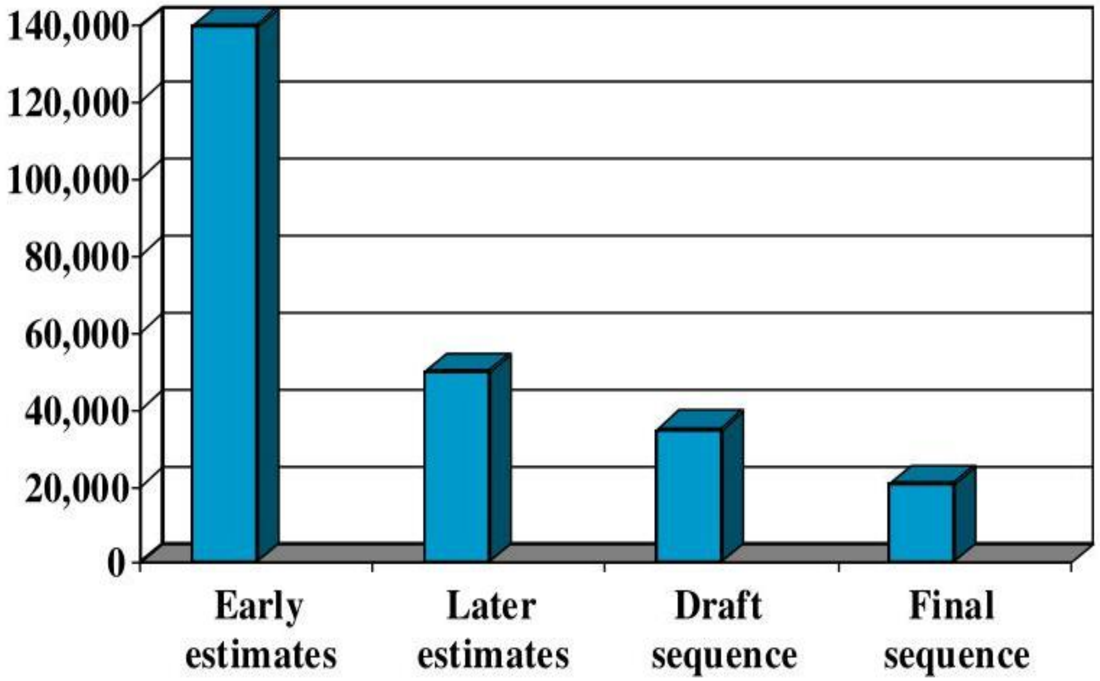
Gene Sequencing

Even knowing the whole DNA sequence doesn't reveal all proteins being made in a cell type.



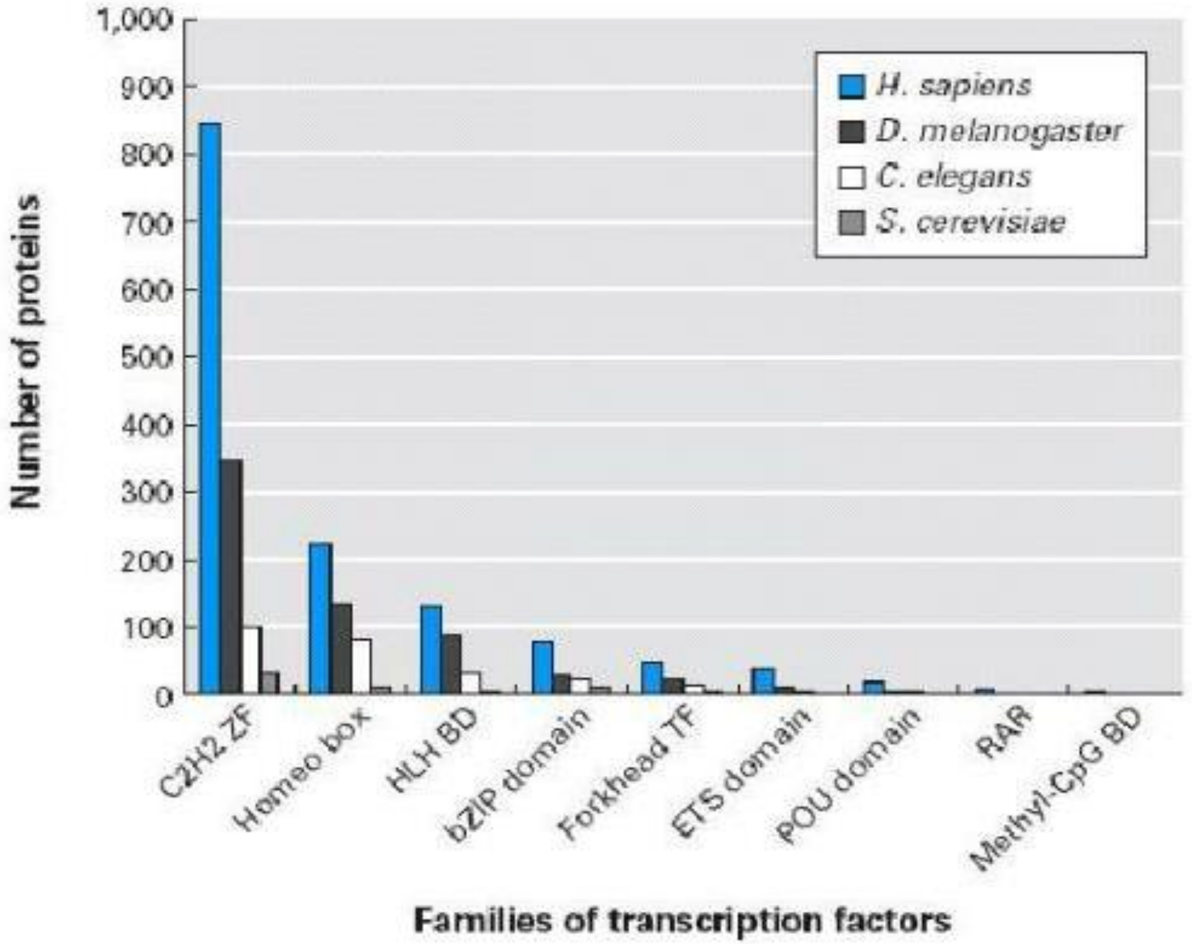
Human Genome Project

The Number of Human Genes



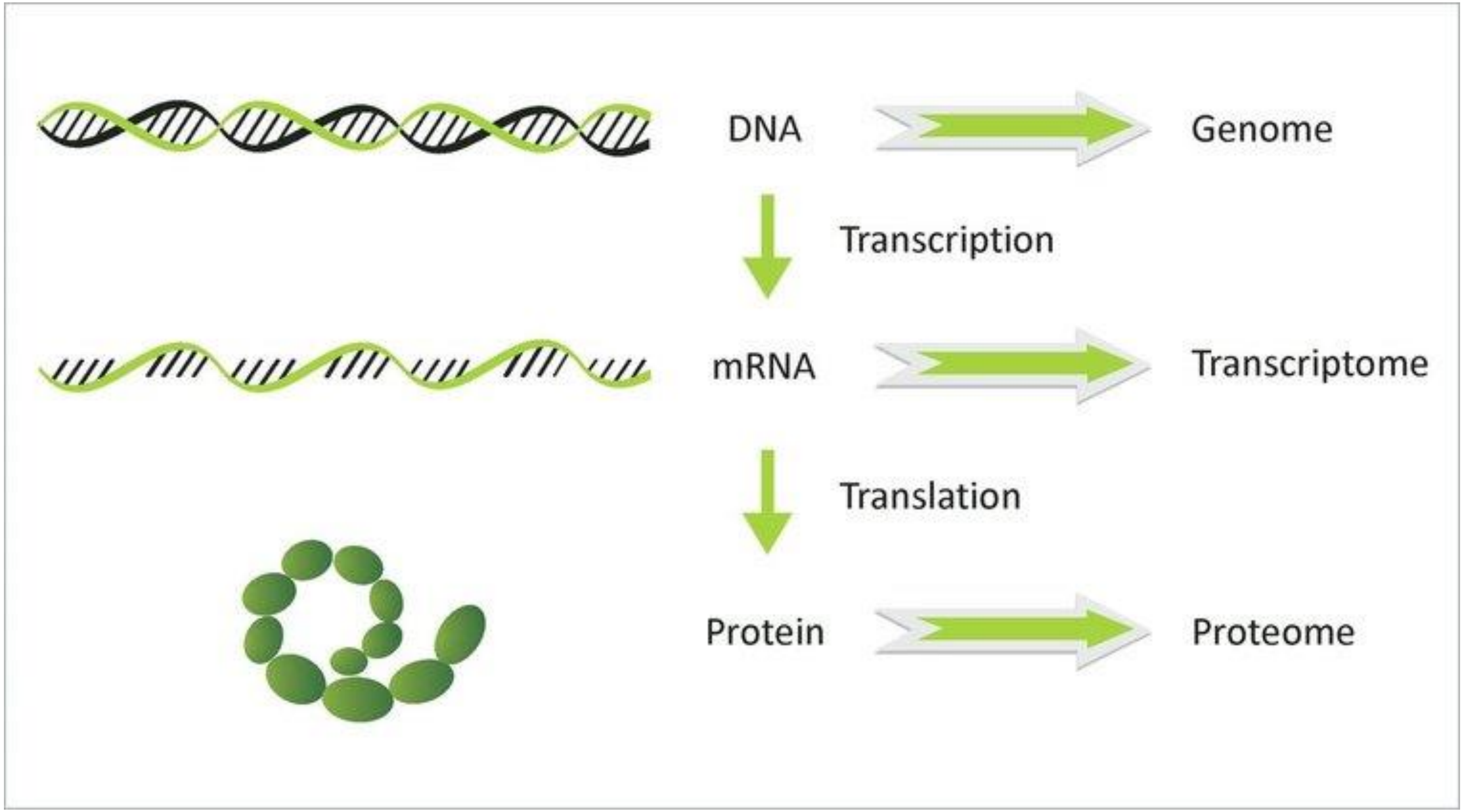
Isoforms (splice variants) counted as one gene

Families of Transcription Factors



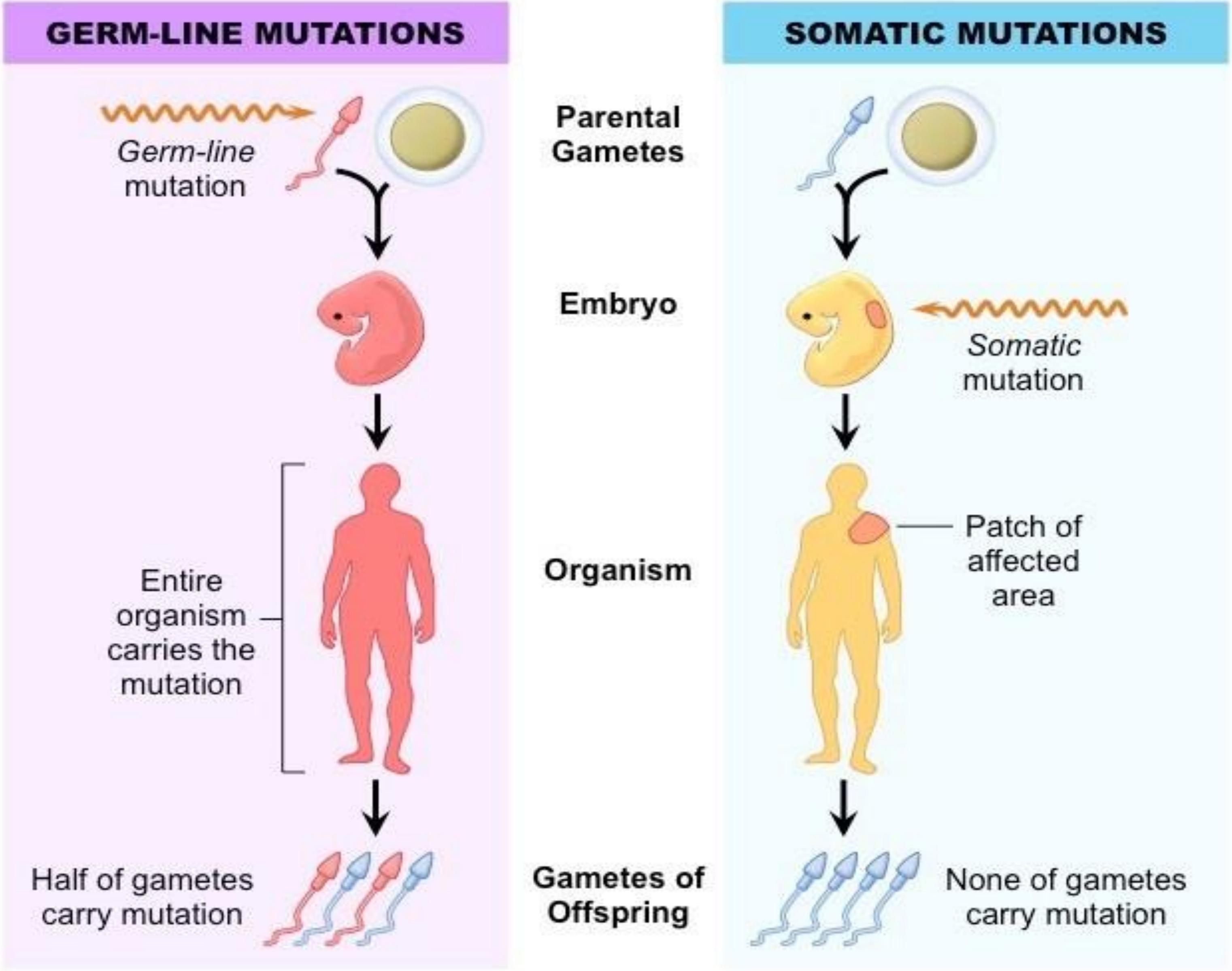
Transcriptome

Can now determine the mRNAs being transcribed for single cells, to see which genes are being expressed in that cell.



Mutations

DNA may be damaged radiation, sunlight, chemicals, chance. Efficient repair mechanisms, but some do persist. May be handed down (germ-line) or affect only the individual (somatic). May be harmless or cause disease by producing damaged or distorted or missing proteins. May affect regulatory genes.
Sickle-cell vs cancer



CRISPR

Clustered regularly interspaced short palindromic repeat sequences