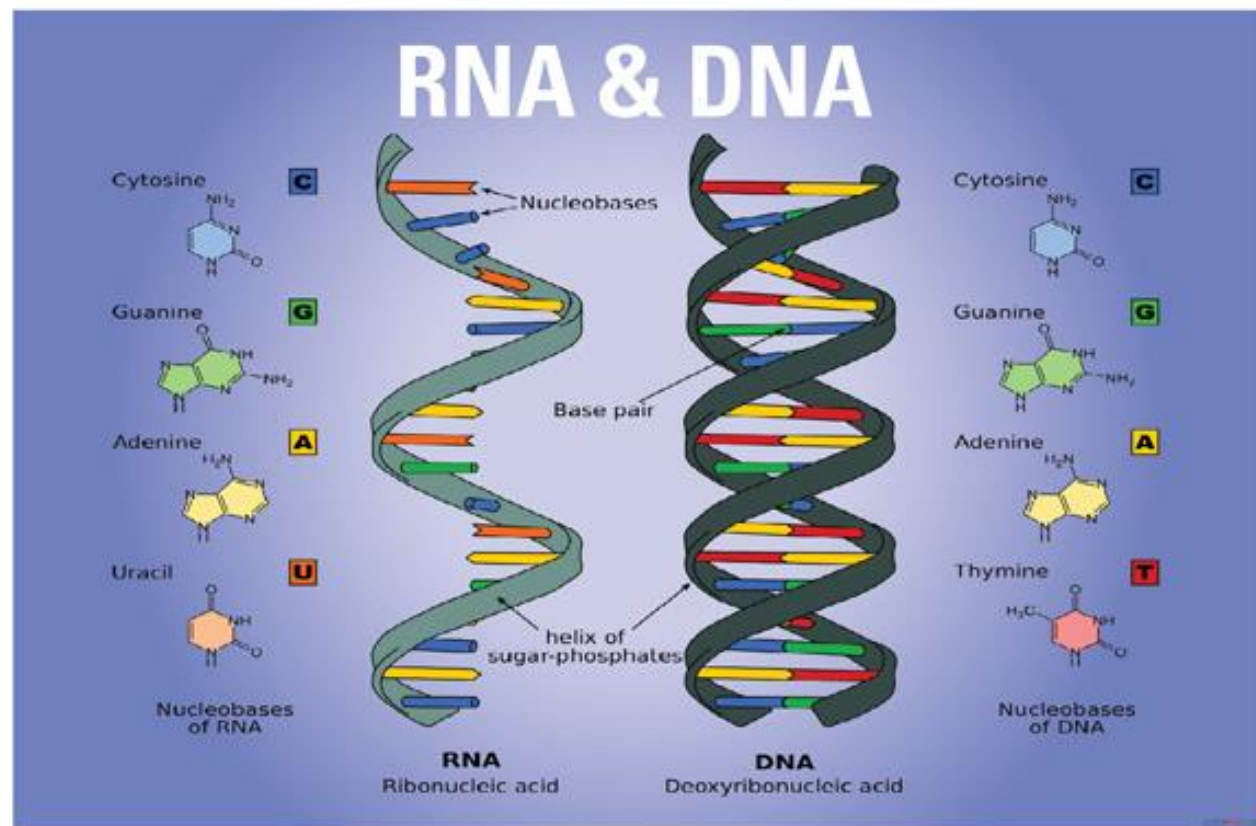


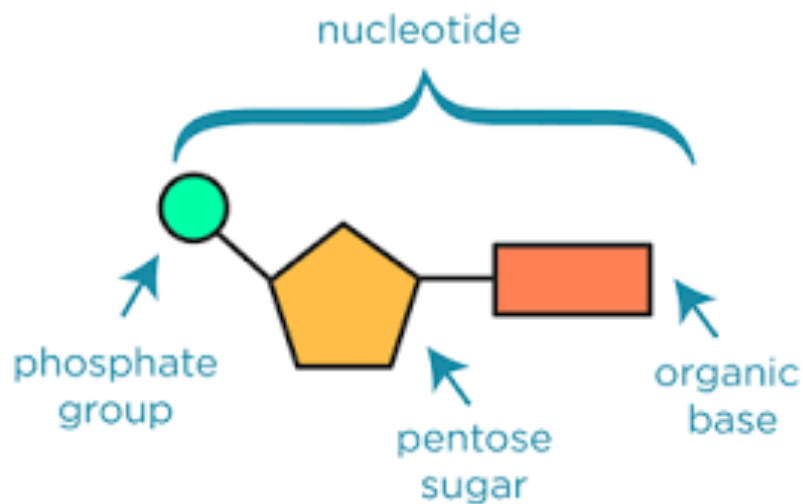
Nucleic acid:
DNA, RNA



Nucleotides: the building blocks of nucleic

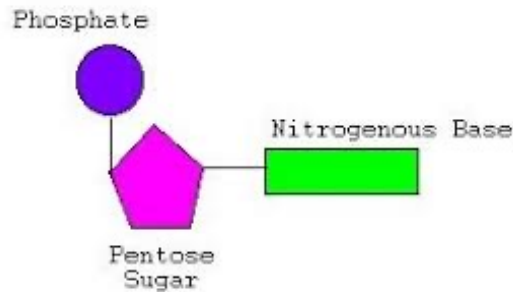
Only 4 types of nucleotides constitutes DNA or RNA

Typical structure



A: Pentose sugar
B: Organic base
C: Phosphate group

Let's build up a nucleotide!

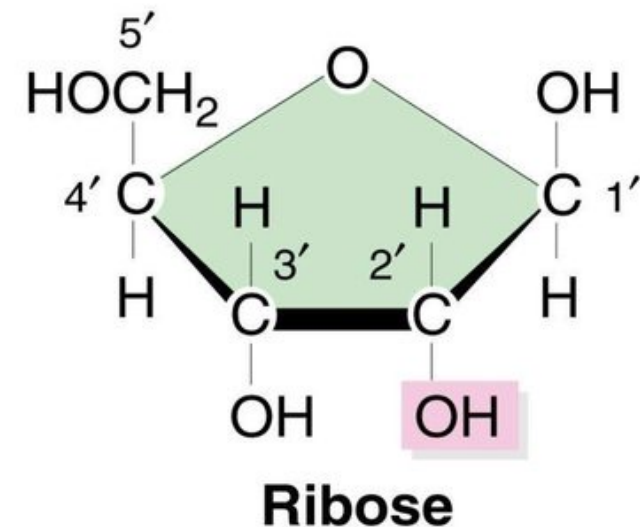
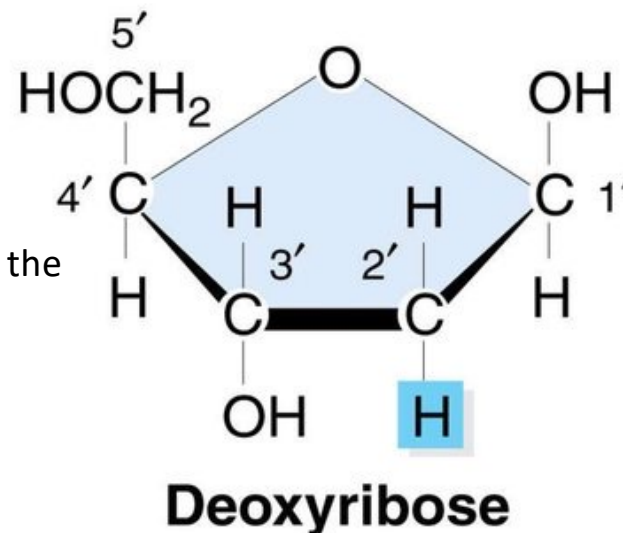


...Let's build up a nucleotide!

Pentose sugar

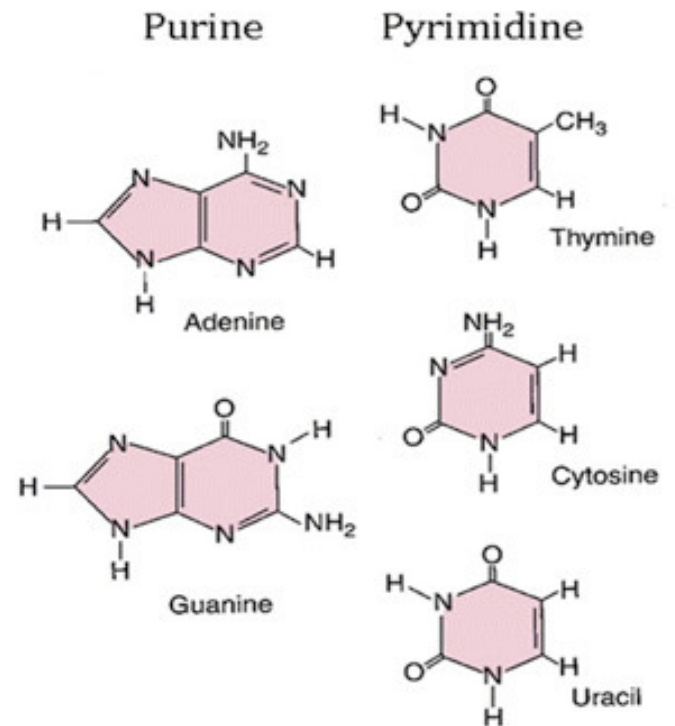
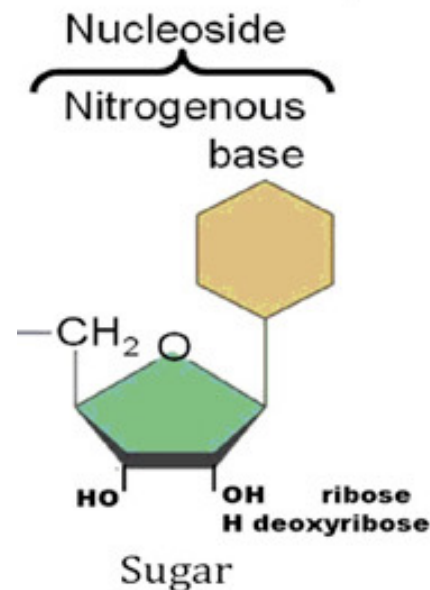
- The pentose (5-carbon) sugar can be either ribose (in RNA) or **deoxyribose (in DNA)**. As their names suggest, deoxyribose is almost the same as ribose, except that it has one fewer oxygen atoms in its molecule.

C1: binds the nitrogenous base
 C5: binds the phosphate group
 C3: binds the phosphate group of the subsequent nucleotide

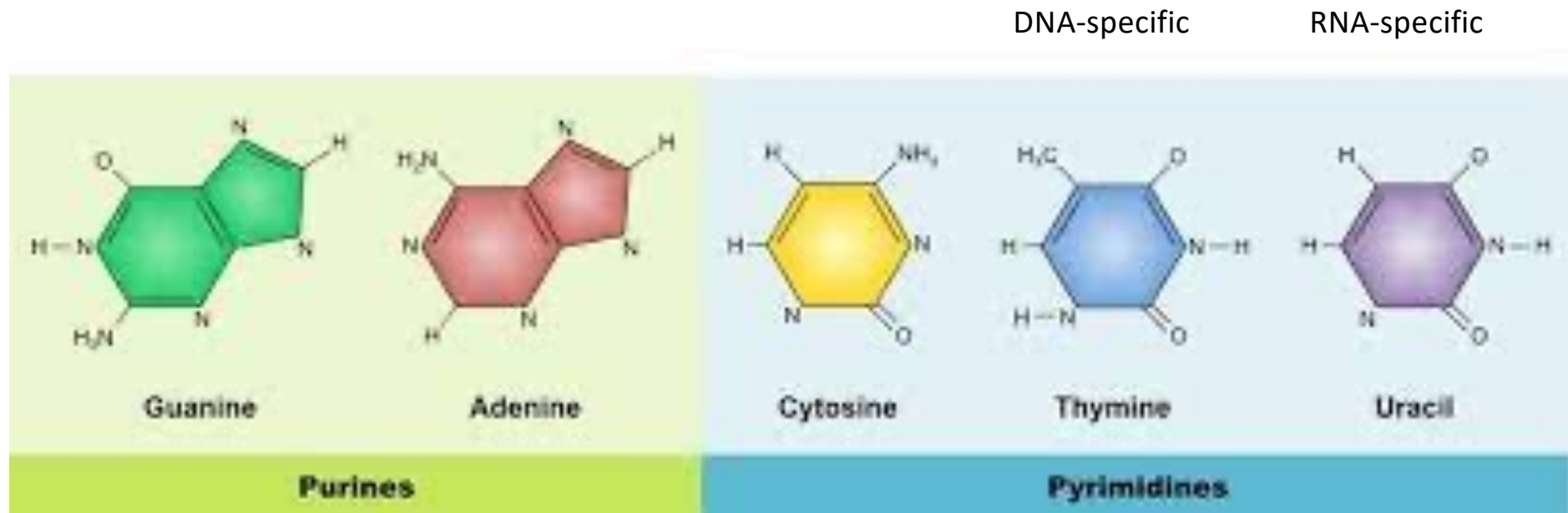


Nucleosides: pentose sugar + nitrogenous base

- Ribonucleoside
- Deoxy-ribonucleoside



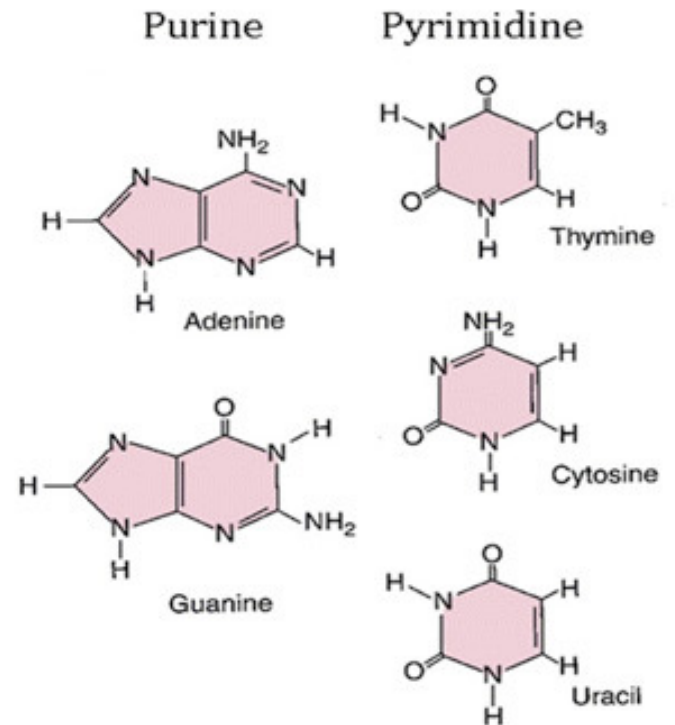
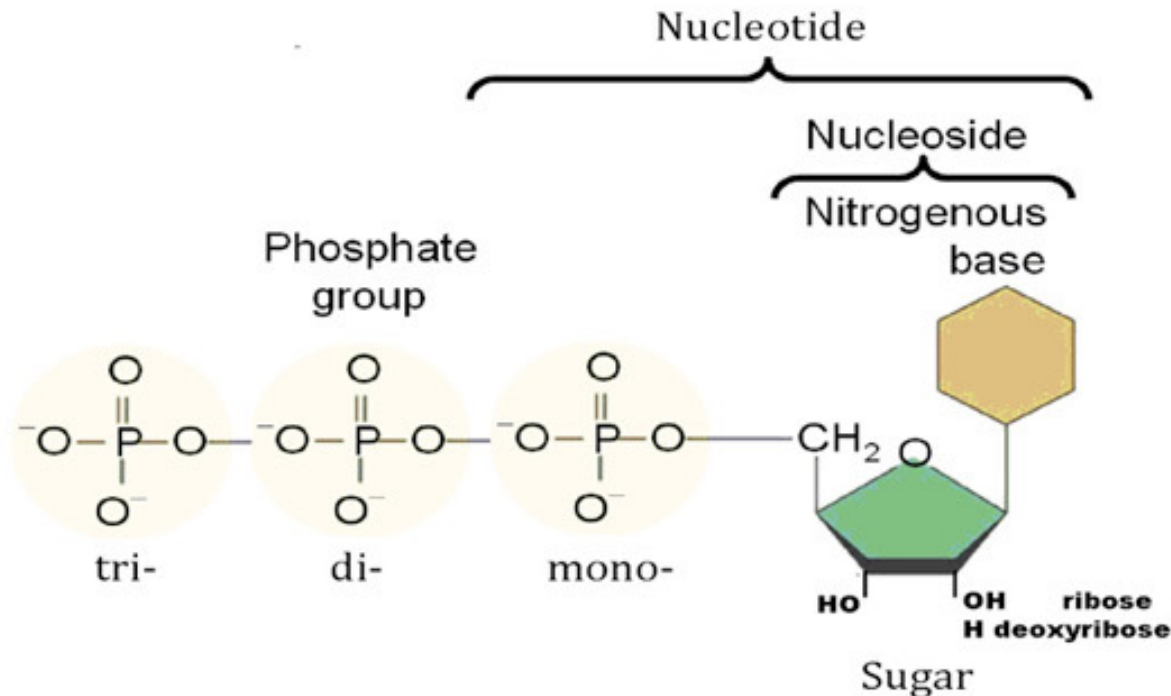
the Nitrogenous bases



Only 4 letters constitute the alphabet of genetic information!

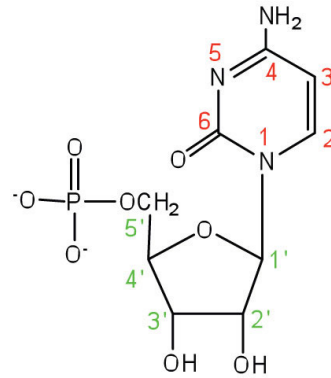
Nucleoside vs nucleotide

- Ribonucleotide
- Deoxy-ribonucleotide

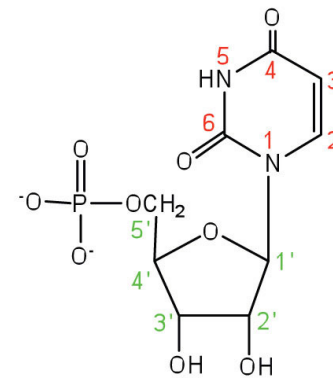


Examples and nomenclature of nucleotides

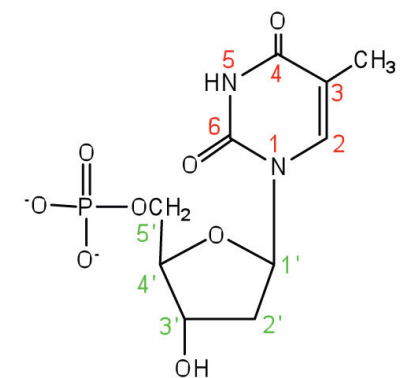
Pyrimidine Nucleotides



Cytidine monophosphate
CMP

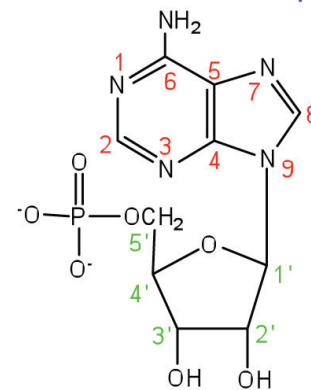


Uridine monophosphate
UMP

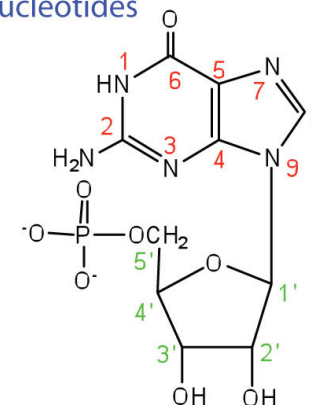


Deoxythymidine monophosphate
dTMP

Purine Nucleotides



Adenosine monophosphate
AMP



Guanosine monophosphate
GMP

Main roles of nucleotides

Monomers of nucleic acids

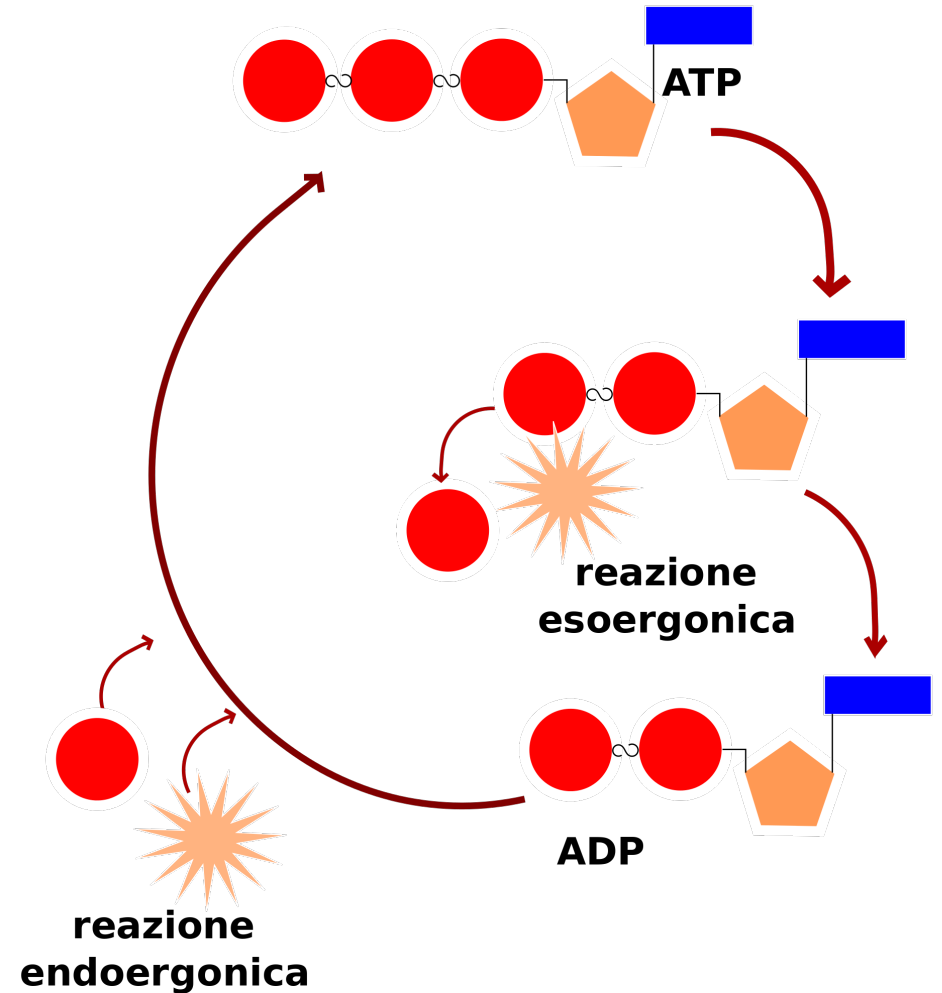
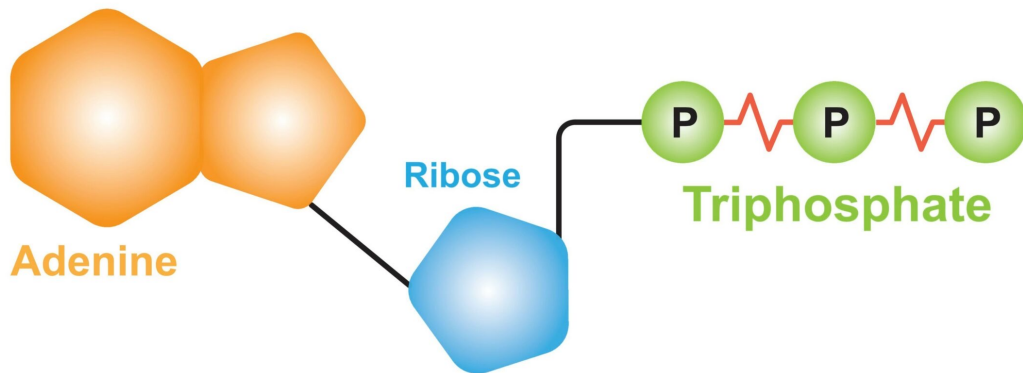
Provide energy for cellular processes

Messengers for signal transduction

Nucleotides as energy deposit

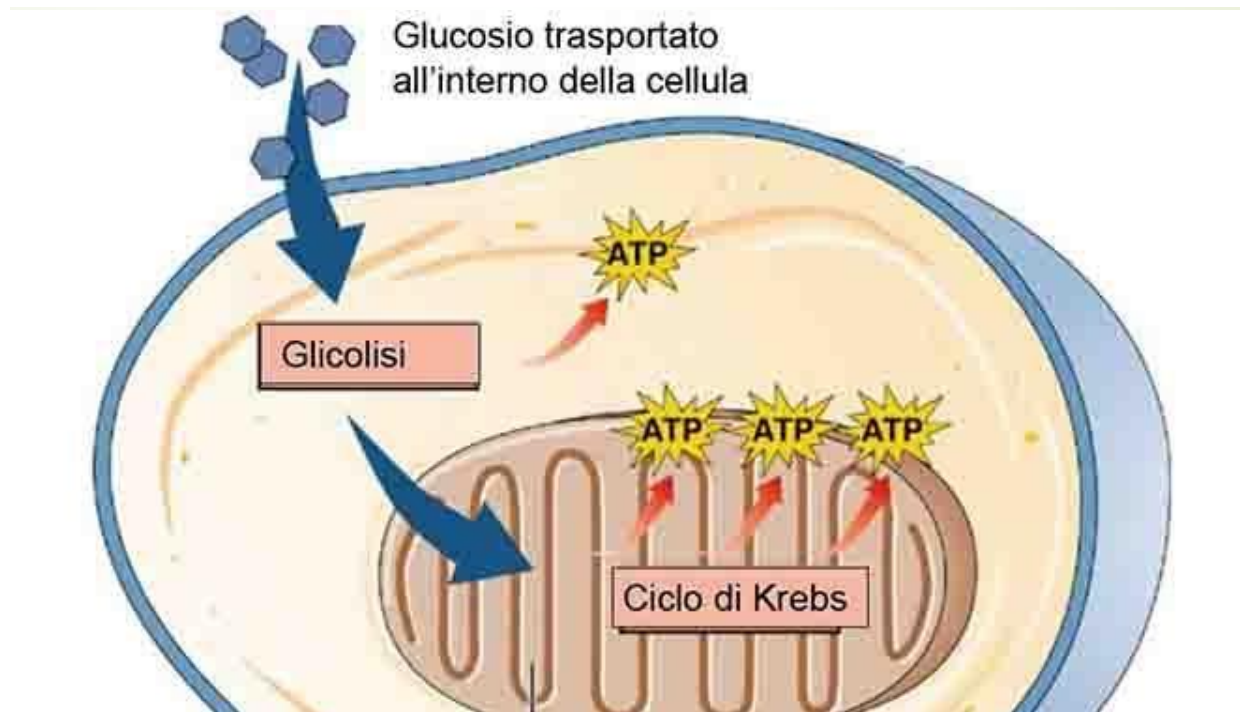
- The chemical bond between phosphates (P-O-P) is the major source of energy in the cell
- When needed ATP and GTP are dephosphorylated, with release of energy
- Same reactions can occur in opposite direction when energy storage is required

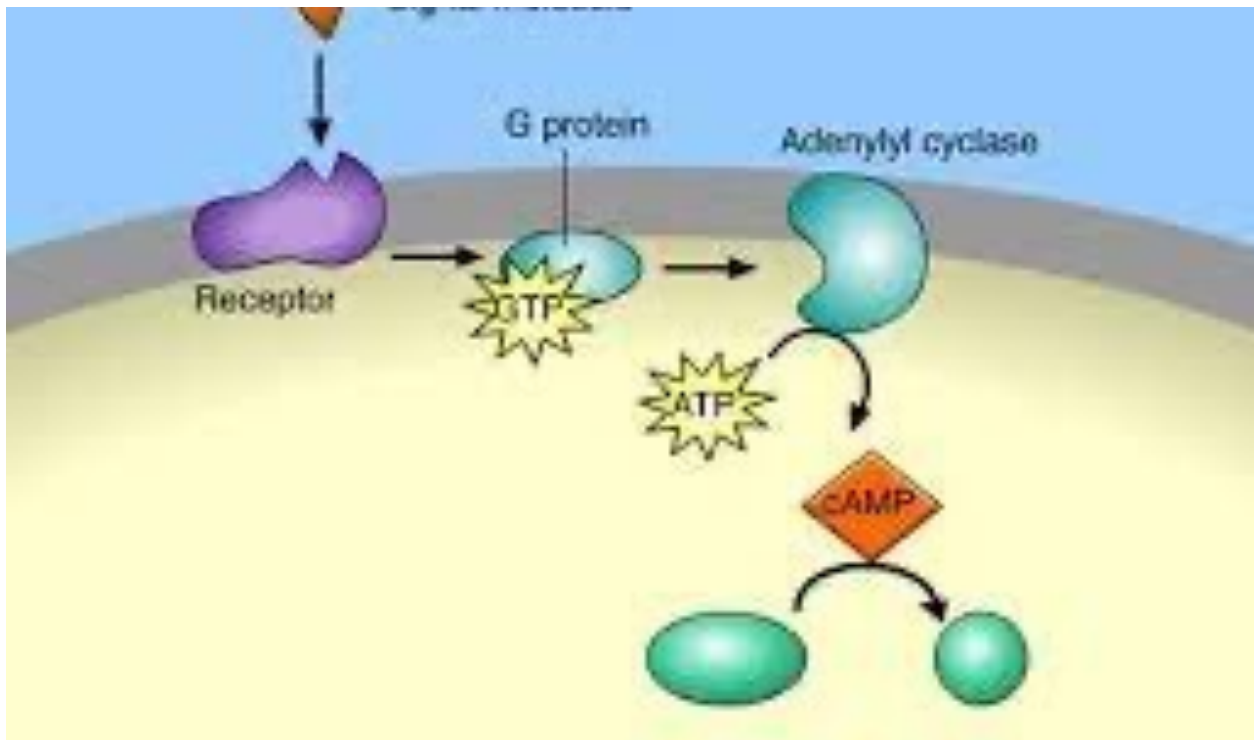
Adenosine triphosphate molecule



Nucleotides as energy deposit

The catabolism of glucose in the cell produces chemical energy that is stored in the form of ATP or GTP





Nucleotides as signaling molecules

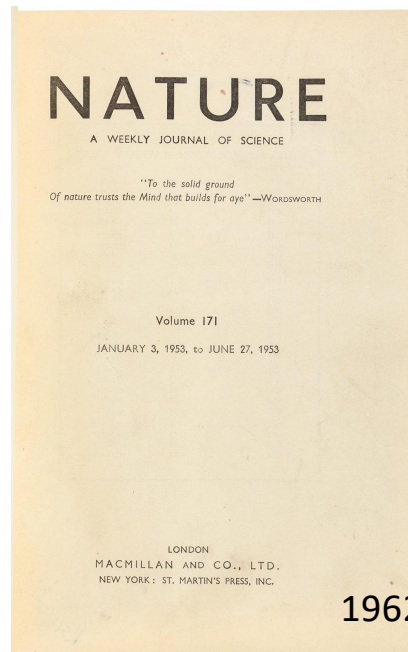
- In response to external signalling, nucleotides such as ATP or GTP are made cyclic and in this shape can activate or deactivate cellular processes

1953:the discovery of DNA structure



The proposed double-helix model revealed:

- That the genetic information is hidden in the sequences of the nitrogenous bases
- The modality through which DNA can self-replicate in daughter cells and thus the way the genetic information could be inherited among generations



1962: Nobel prize was assigned to Crick, Watson, Wilkins

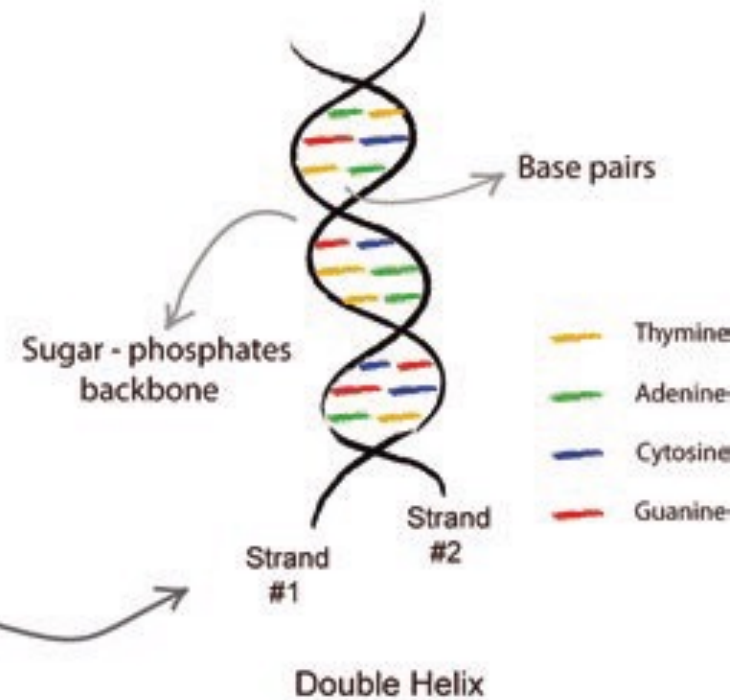
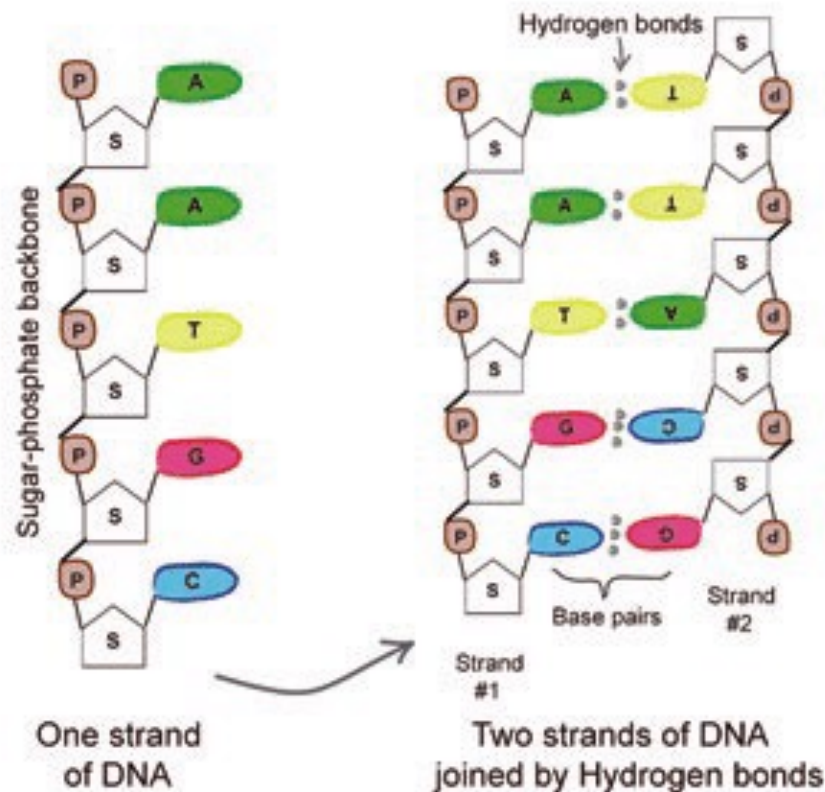
The structure of DNA

Deoxyribonucleic acid (DNA) is made of two complementary chains of Deoxyribonucleotides.

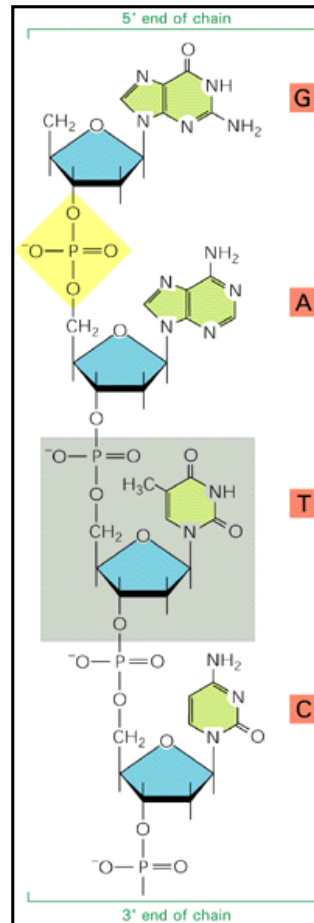
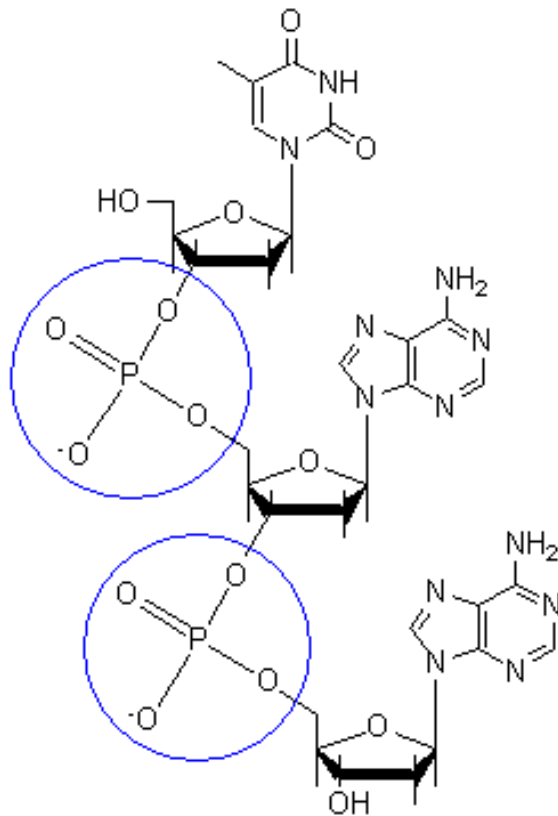
A Nucleotide



B DNA molecule



The phosphodiester bond in a polynucleotide chain:

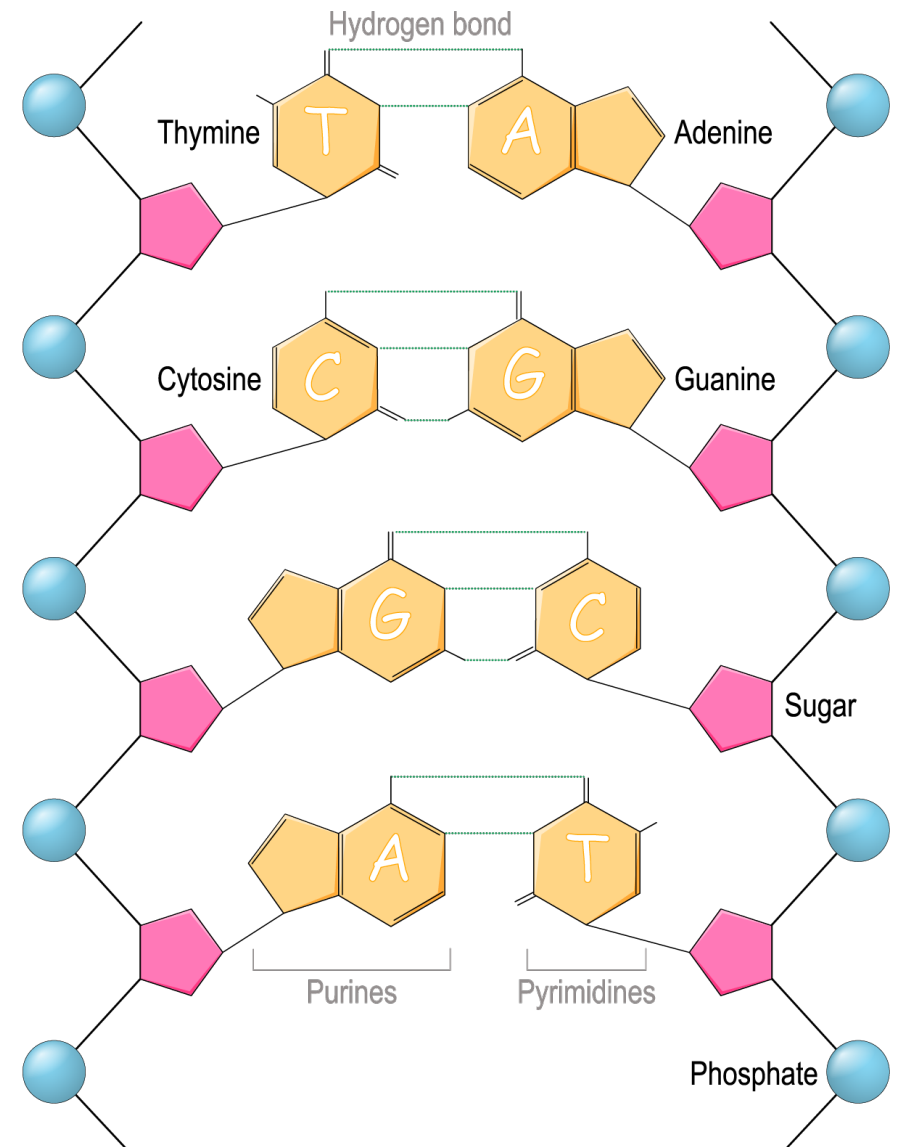
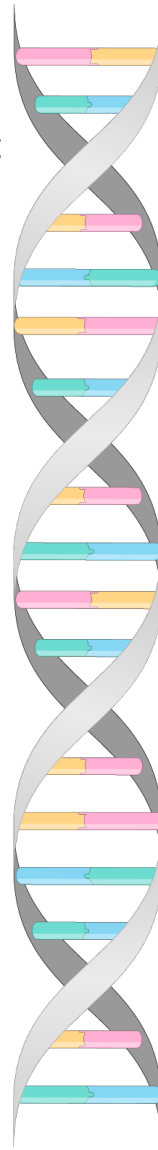


- One molecule of phosphoric acid bridges C3 of one nucleotide and C5 of the other.
- Polynucleotide chain grow ALWAYS from 5' to 3' direction

How is the double helix formed?

The DNA molecule consists of two strands that wind around one another to form a shape known as a double helix. Each strand has a backbone made of alternating sugar (deoxyribose) and phosphate groups. Attached to each sugar is one of four bases--adenine (A), cytosine (C), guanine (G), and thymine (T).

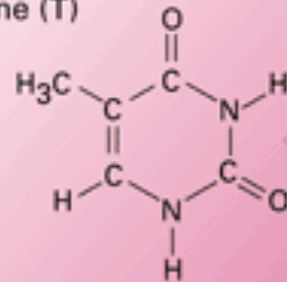
The two strands are held together by bonds between the bases,, according to [base pairing](#) rules (A with T and C with G), with [hydrogen bonds](#) to make double-stranded DNA. The sequence of the bases along the backbones serves as instructions for assembling protein and RNA molecules.



Nitrogenous
bases interact
with each other
complementarily

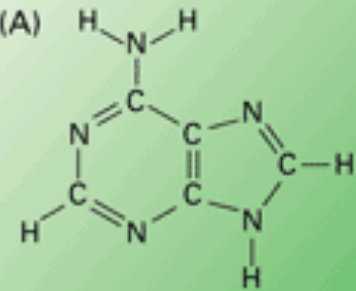
Pyrimidines

Thymine (T)

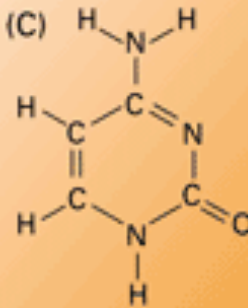


Purines

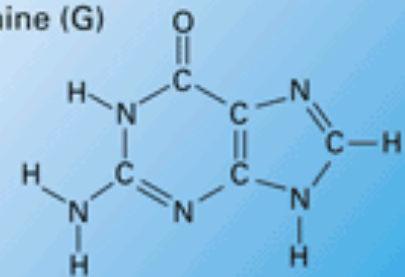
Adenine (A)



Cytosine (C)



Guanine (G)



The structure of DNA

The chains coil around each other to form a double helix, with constant diameter and a major and minor grooves.

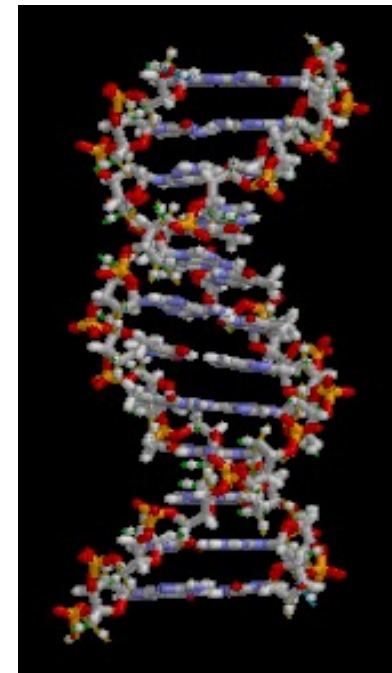
Properties of DNA:

The two strands of DNA run in opposite directions to each other and are thus [antiparallel](#).

The two strands are [complementary](#) to each other, one strand predicts the other

The double helix is hydrophilic (and [acidic](#)) on the surface, while hydrophobic internally

The sequence of the bases along the backbones serves as instructions for assembling protein and RNA molecules

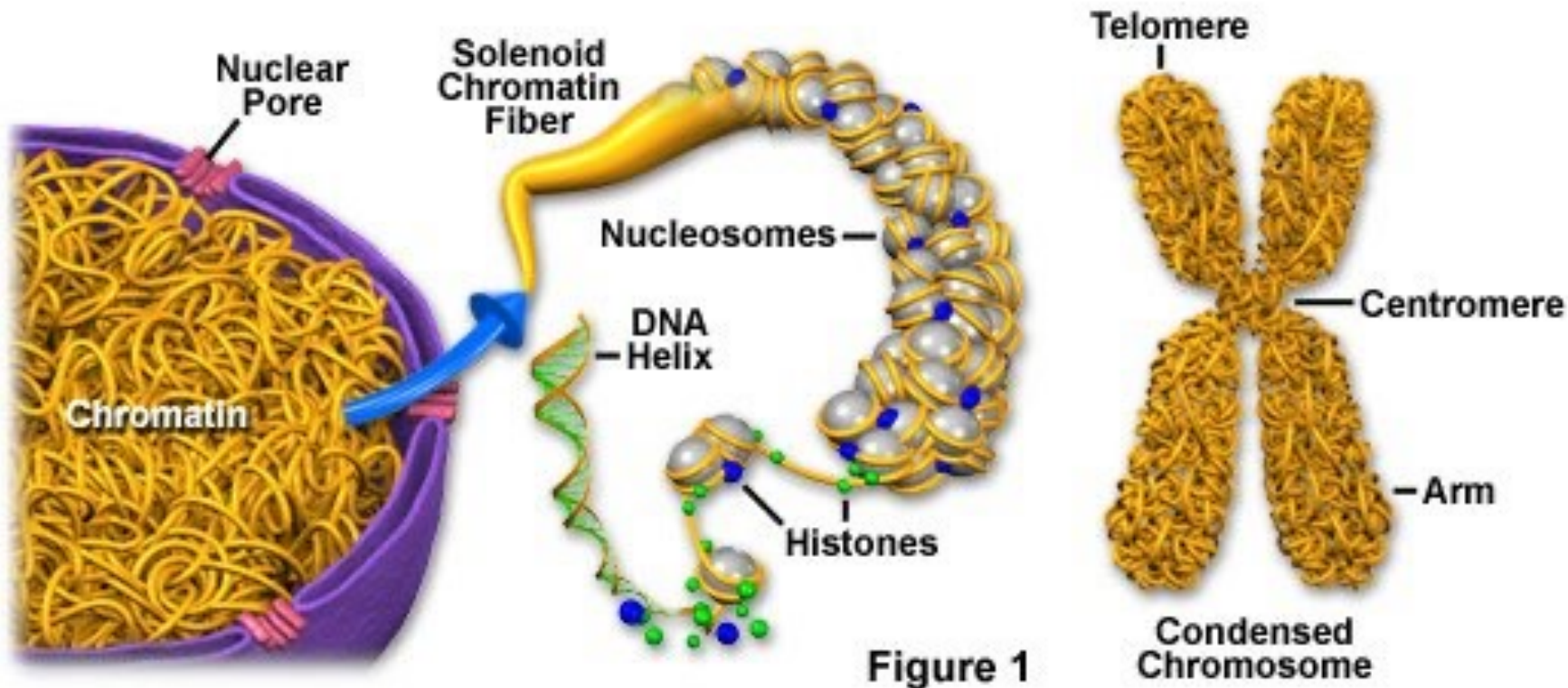


At actual size, a human cell's DNA totals about **3 meters** in length!!

DNA is organized into chromatin in eukaryotic cells

Chromatin primary function is to package long DNA molecules into more compact, denser structures. This prevents the strands from becoming tangled and also plays important roles in regulating [gene expression](#) and [DNA replication](#).

Chromatin and Condensed Chromosome Structure

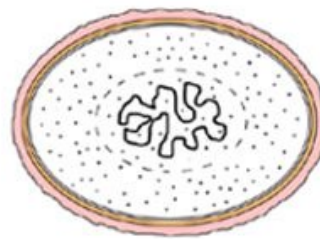


Two Basic Cell Types: Prokaryotic vs. Eukaryotic Cells

Eukaryotic cells contain a nucleus

IN Eukaryotic cells, DNA is long and supercoiled around histone proteins to form chromatin.

In Prokaryotic cells, DNA is short, in a linear circular molecule, directly in cytoplasm and with no chromatin

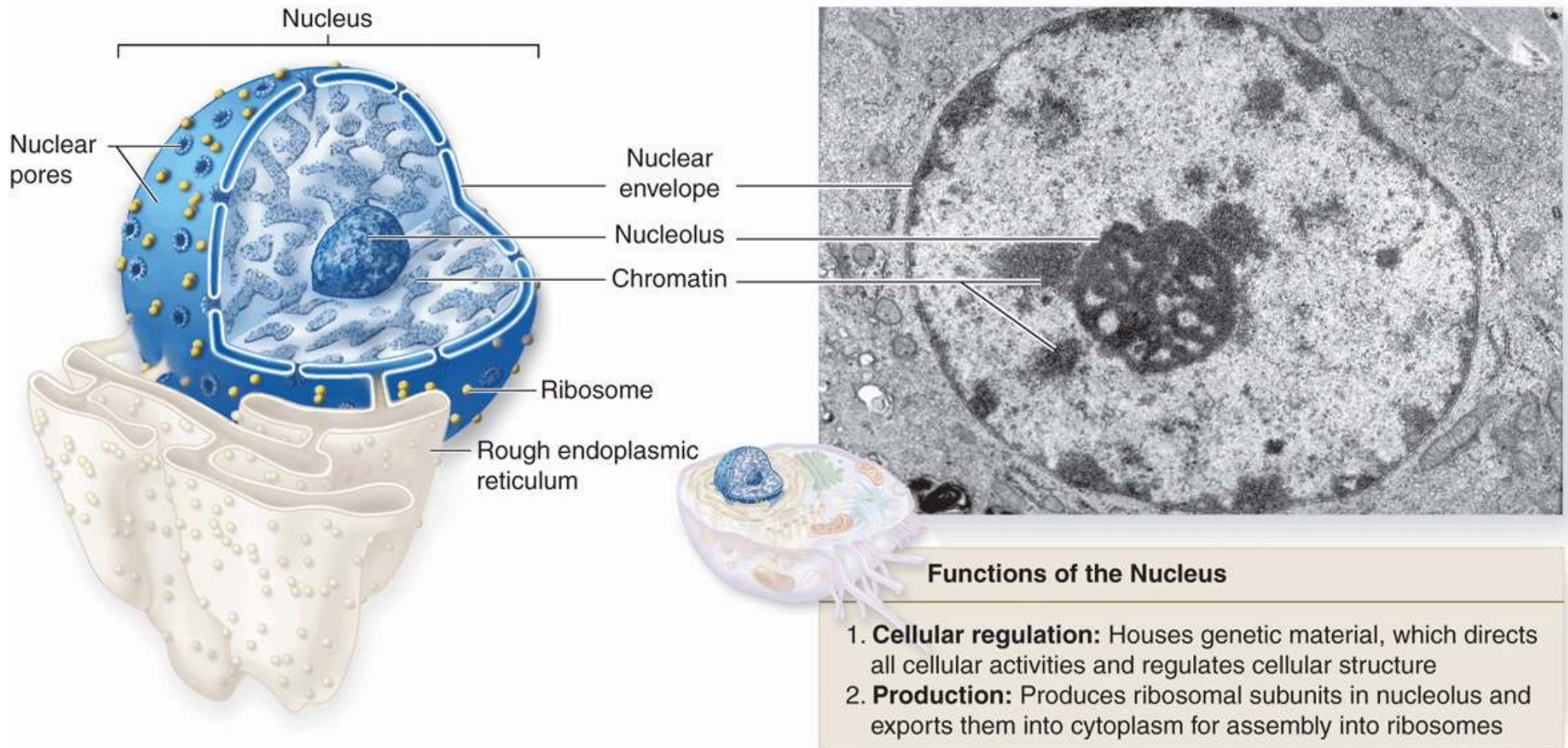


Prokaryotic Cell

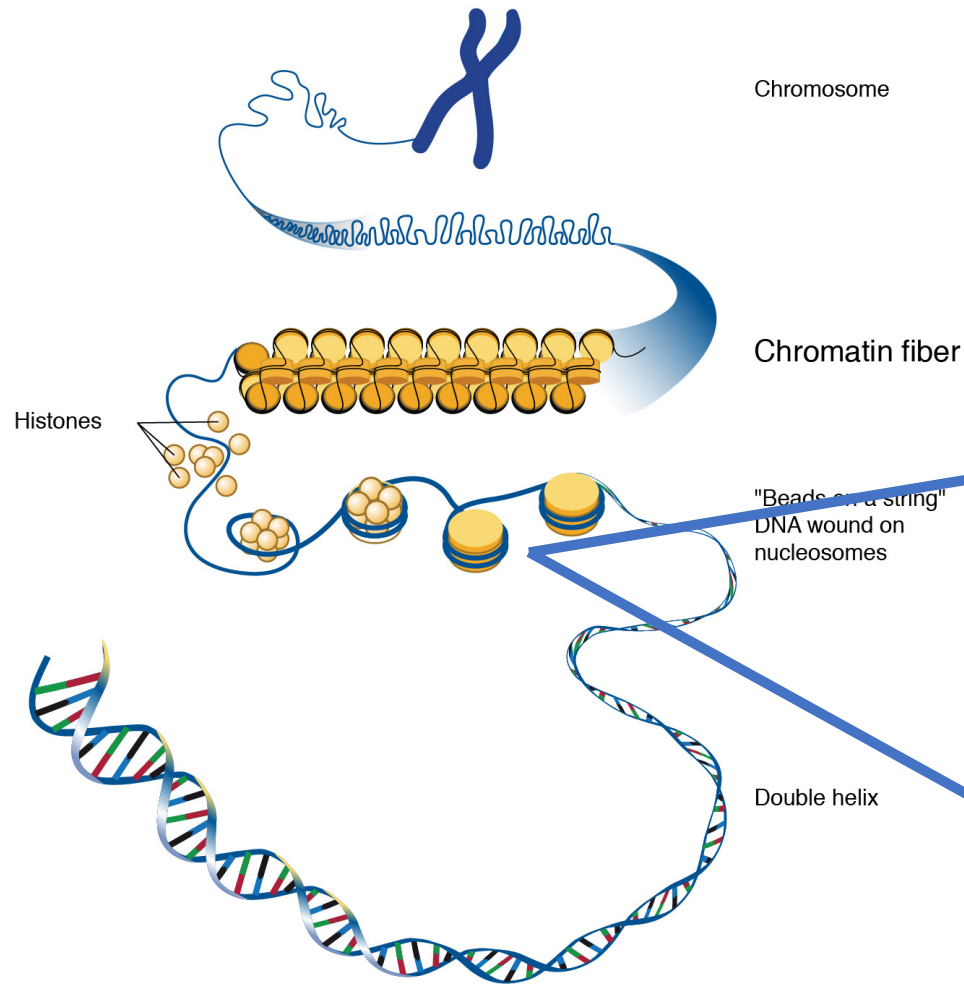


Animal (Eukaryotic) Cell

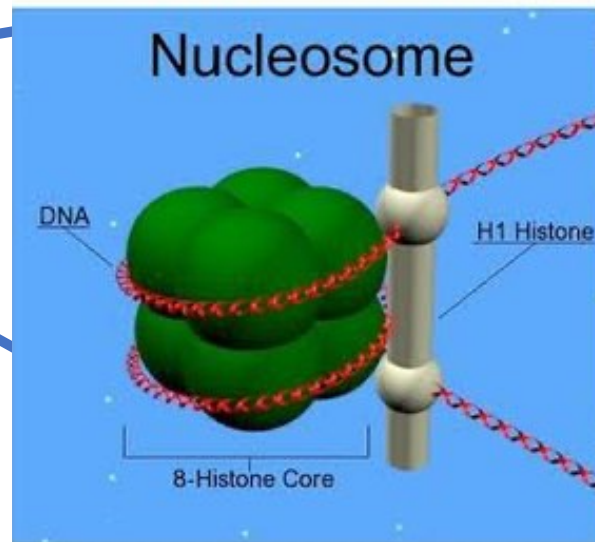
Chromatin is contained in cell nucleus



The primary protein components of chromatin are [histone proteins](#).



histones are highly [basic proteins](#) abundant in [lysine](#) and [arginine](#) residues that act as spools around which [DNA](#) winds to create structural units called [nucleosomes](#).

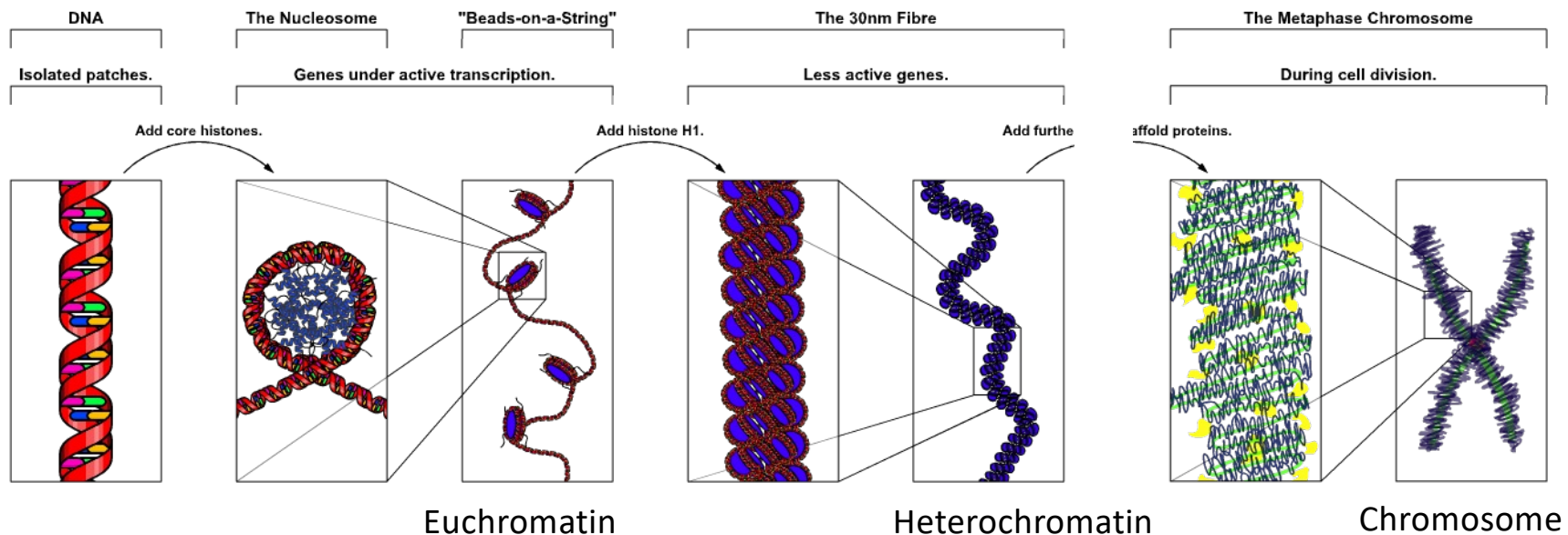


- DNA is wrapped around collections of proteins called histones
- Histones carry a positive charge and DNA carries a negative charge, so they are held together by electrostatic attraction
- 9 histones with DNA coiled twice around the 8 histone core is called a nucleosome

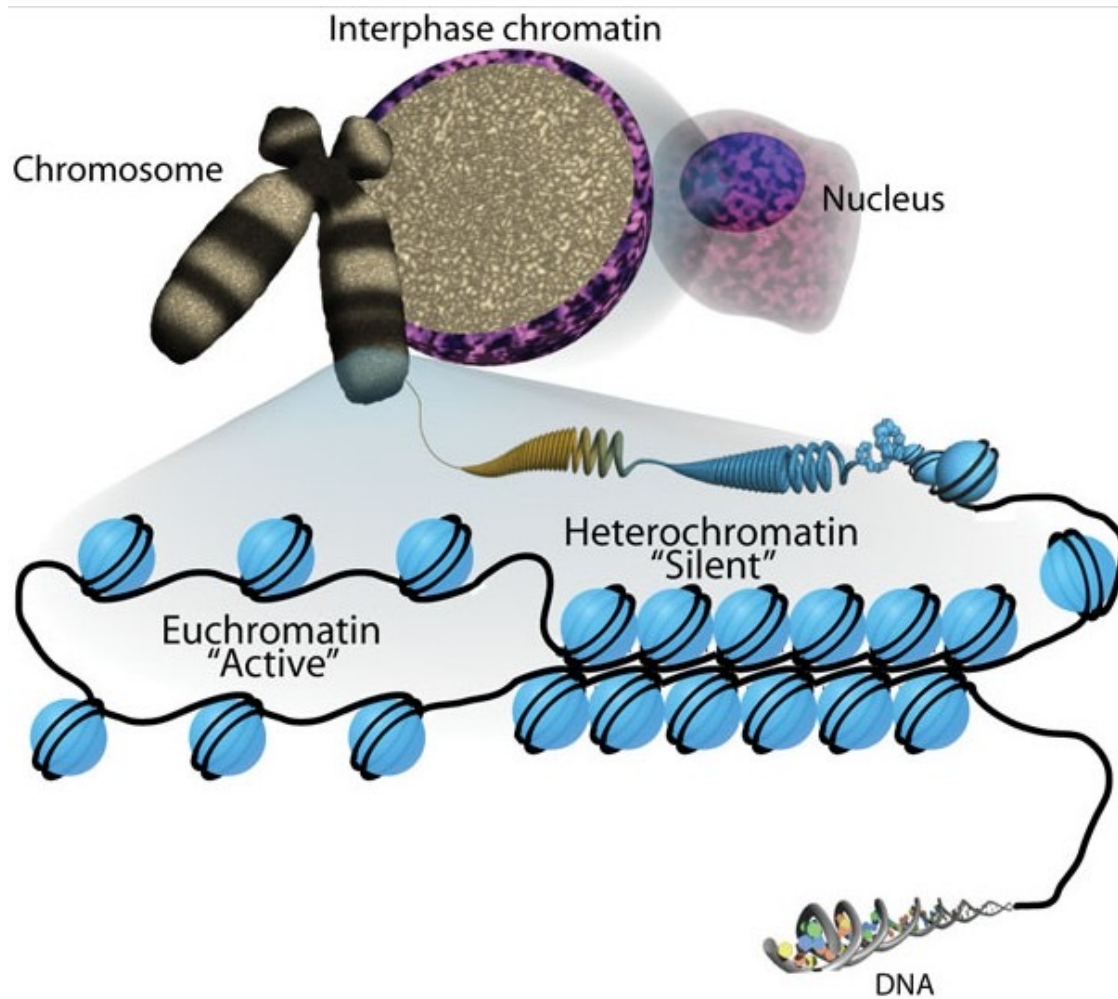
Chromatine is a dynamic structure

In general, there are three levels of chromatin organization:

1. DNA wraps around histone proteins, forming nucleosomes and the so-called beads on a string structure (euchromatin).
2. Multiple histones wrap into a 30-nanometer fiber consisting of nucleosome arrays in their most compact form (heterochromatin).
3. Higher-level DNA supercoiling of the 30-nm fiber produces the metaphase chromosome (during cell division).



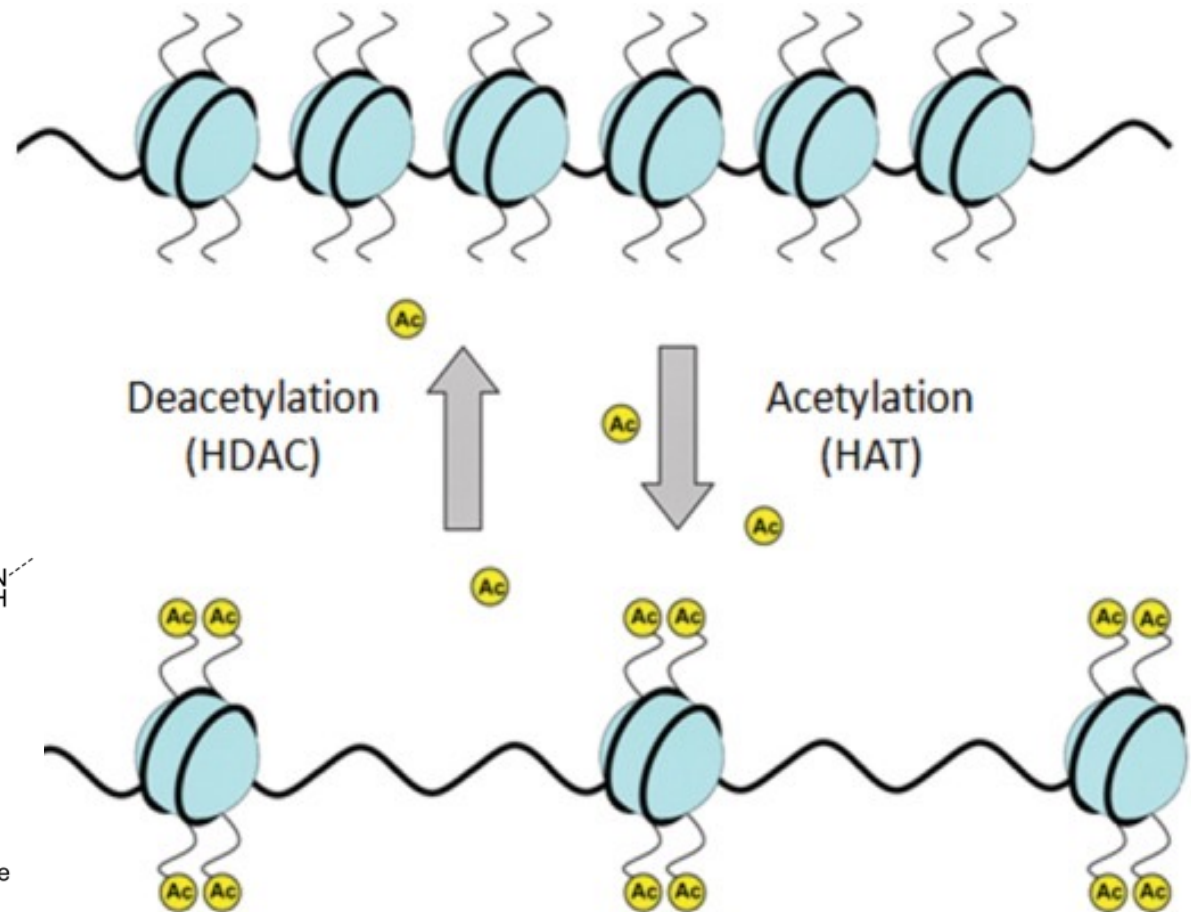
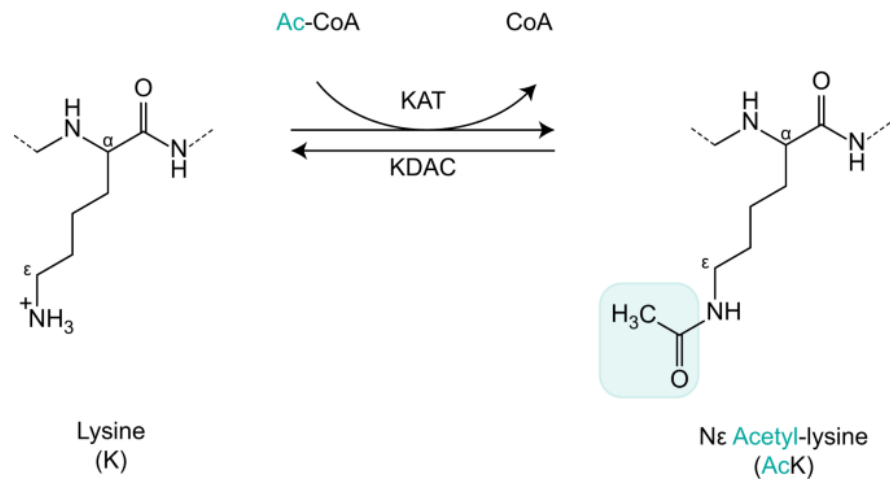
Chromatin remodeling mechanisms change the conformation from Eu- to Hetero-chromatin and viceversa



During the life of the cell (Between two cells division – Interphase), DNA is structured in euchromatin (active) and heterochromatin (silent)

The role of histone modifications in chromatin remodeling

Histone modifications (Acetylation, methylation, phosphorylation) can reduce the electrical attraction between positively charged histones and negatively charged DNA.



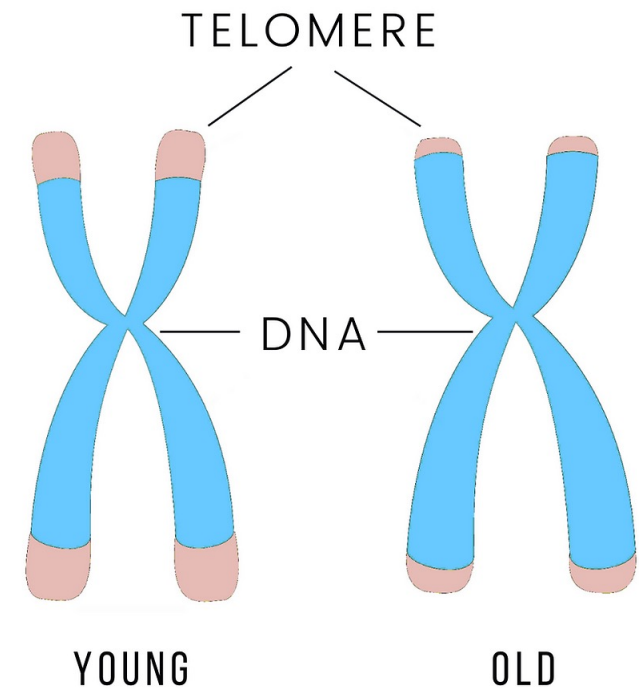
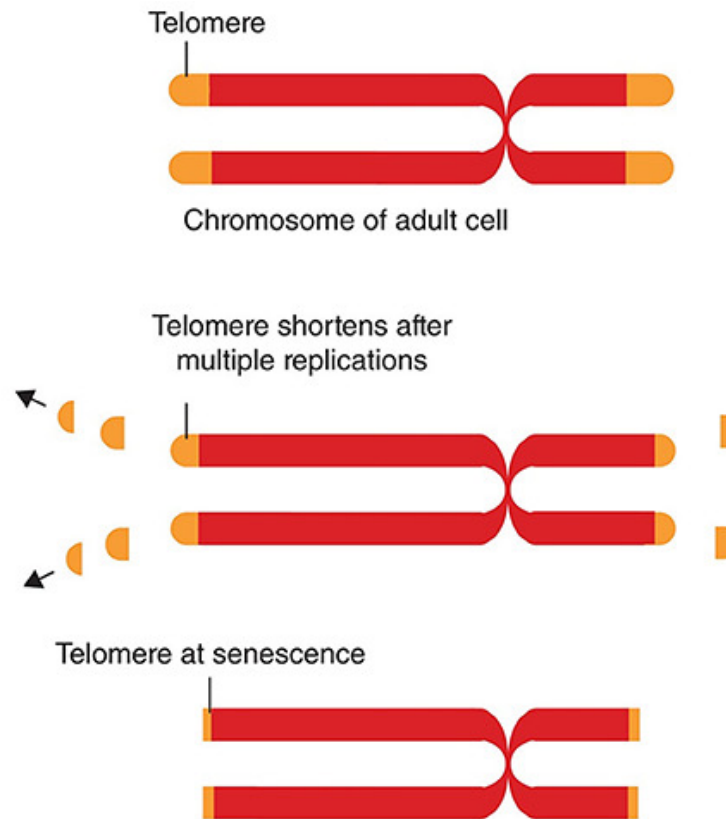
Chromosomes



During cell division chromatin DNA organizes in dense structures called [chromosomes](#). Each chromosome is one DNA molecule. In humans there are 46 chromosomes in each cell (23 couples). The entire chromosome set is defined Karyotype.

Telomeres as measure of aging

Telomeres are region of repetitive nucleotide sequences at the ends of linear chromosomes. They protect the terminal regions of chromosomal DNA from progressive degradation



VIT&DRIP



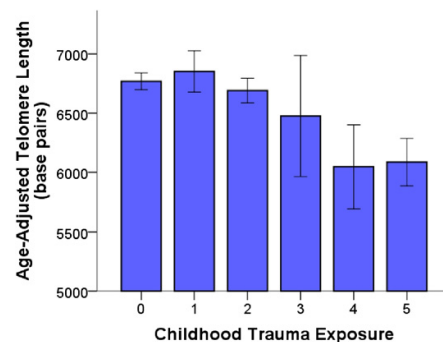
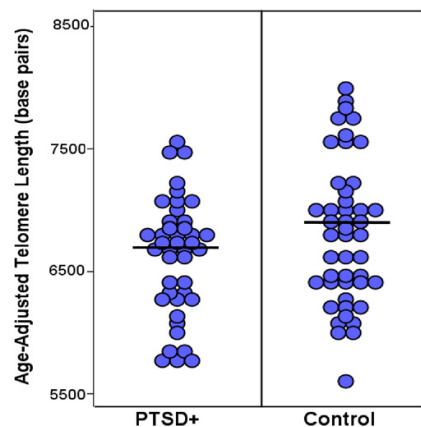
Telomere length predicts the risk for mental disease in early traumatized individuals

Psychiatry Research 246 (2016) 95–100

Childhood Trauma Associated with Short Leukocyte Telomere Length in Posttraumatic Stress Disorder

Aoife O'Donovan, Elissa Epel, Jue Lin, Owen Wolkowitz, Beth Cohen, Shira Maguen, Thomas Metzler, Maryann Lenoci, Elizabeth Blackburn, and Thomas C. Neylan

Conclusions: Childhood trauma is associated with short LTL in individuals with PTSD. Chronic exposure to the psychobiological sequelae of childhood trauma could increase risk for PTSD and short LTL. Thus, the lasting psychological impact of exposure to trauma in childhood might be accompanied by equally enduring changes at the molecular level.



Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres



Accelerated telomere shortening: Tracking the lasting impact of early institutional care at the cellular level



Kathryn L. Humphreys^a, Kyle Esteves^a, Charles H. Zeanah^a, Nathan A. Fox^b, Charles A. Nelson III^c, Stacy S. Drury^{a,*}

Aas et al. *Translational Psychiatry* (2019)9:97
<https://doi.org/10.1038/s41398-019-0432-7>

Translational Psychiatry

ARTICLE

Open Access

Telomere length is associated with childhood trauma in patients with severe mental disorders

Monica Aas¹, Torbjørn Elvsåshagen^{1,2}, Lars T. Ingrid Melle¹, Dennis van der Meer¹, Carmen

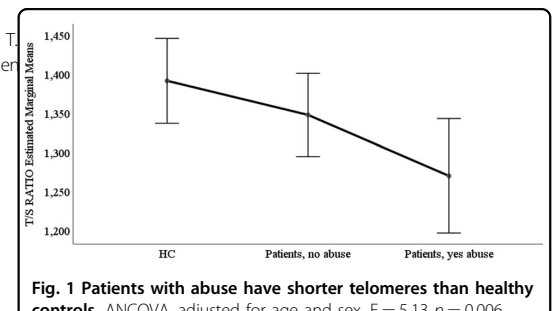
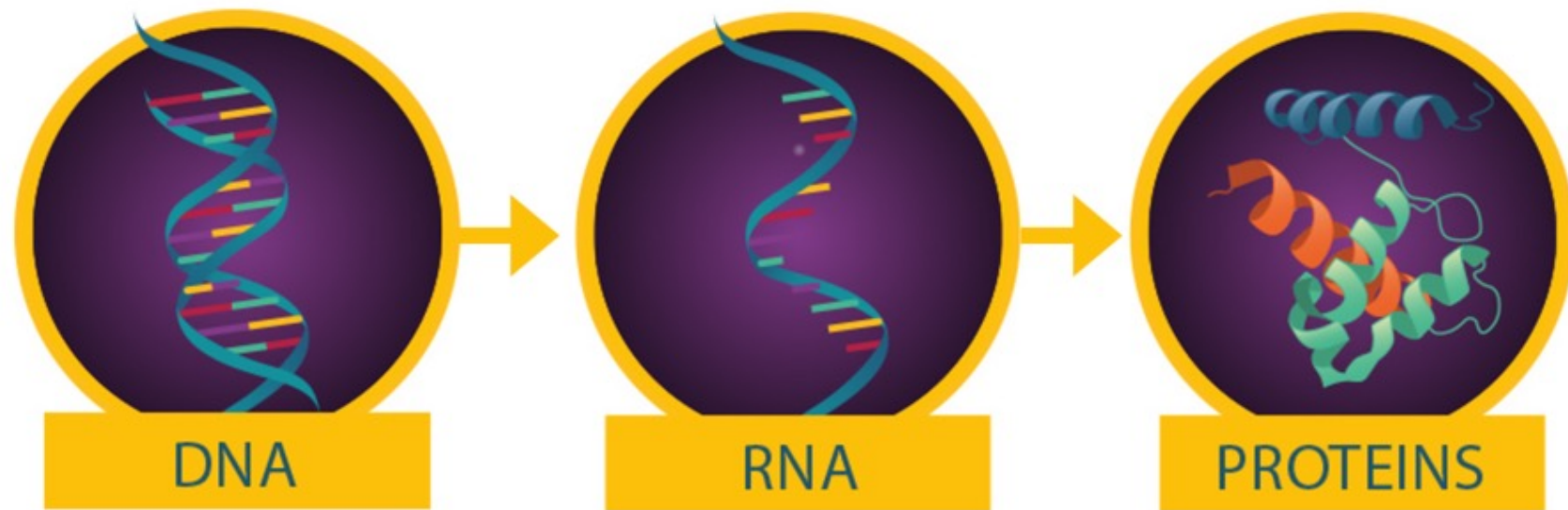


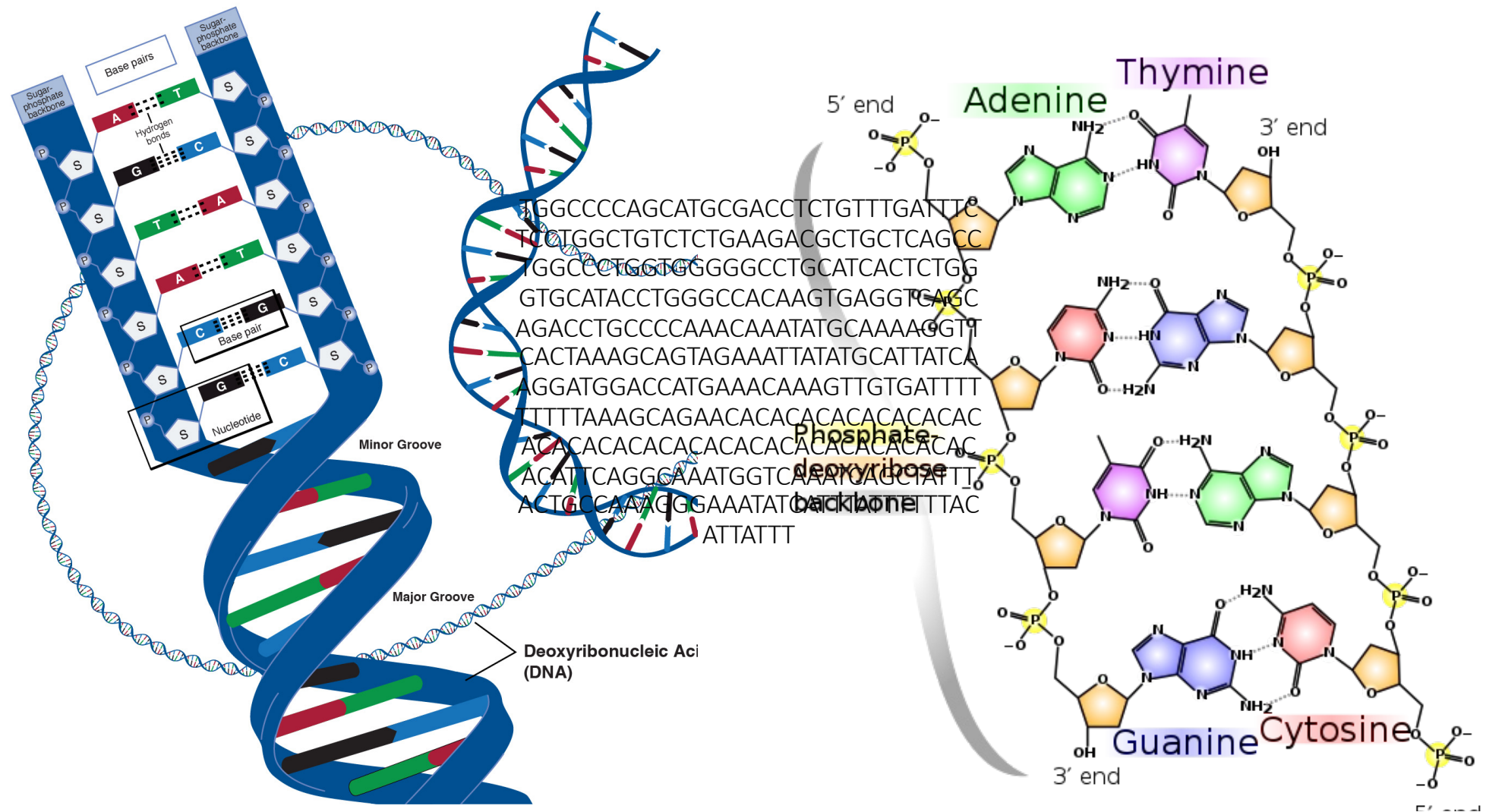
Fig. 1 Patients with abuse have shorter telomeres than healthy controls. ANCOVA adjusted for age and sex: $F = 5.13$, $p = 0.006$.

The sequence of DNA bases contains a message...



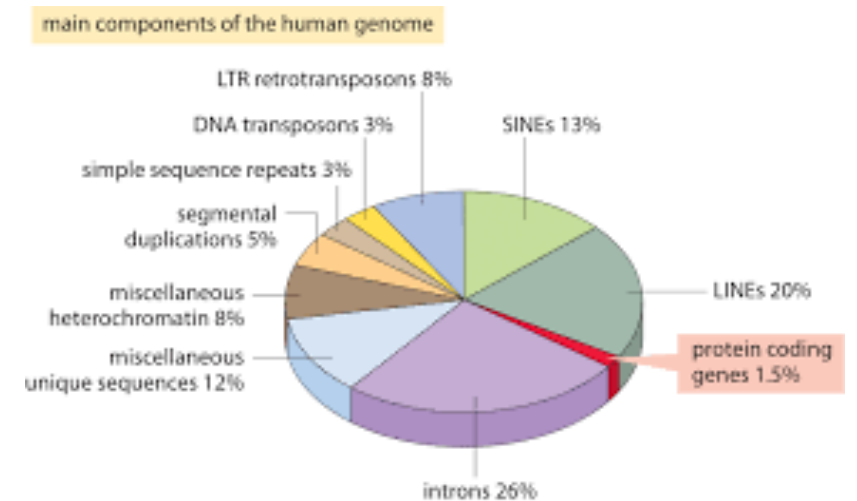
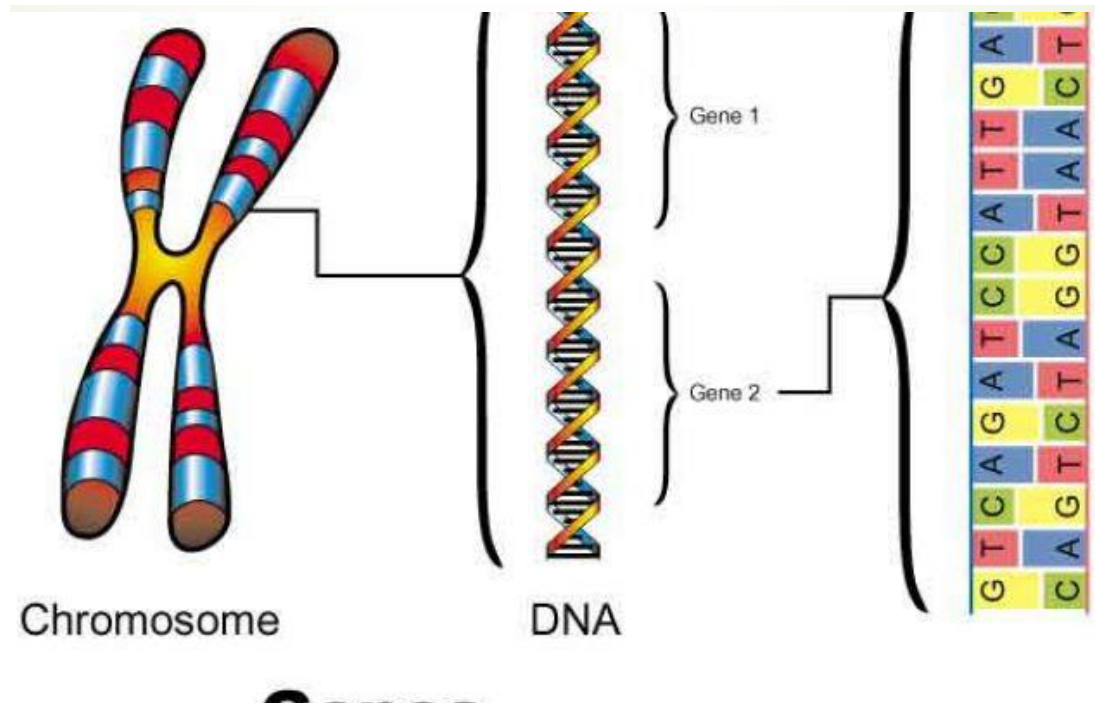
The central dogma of biology

A DNA sequence is described by the sequence of its bases from 5' to 3'.



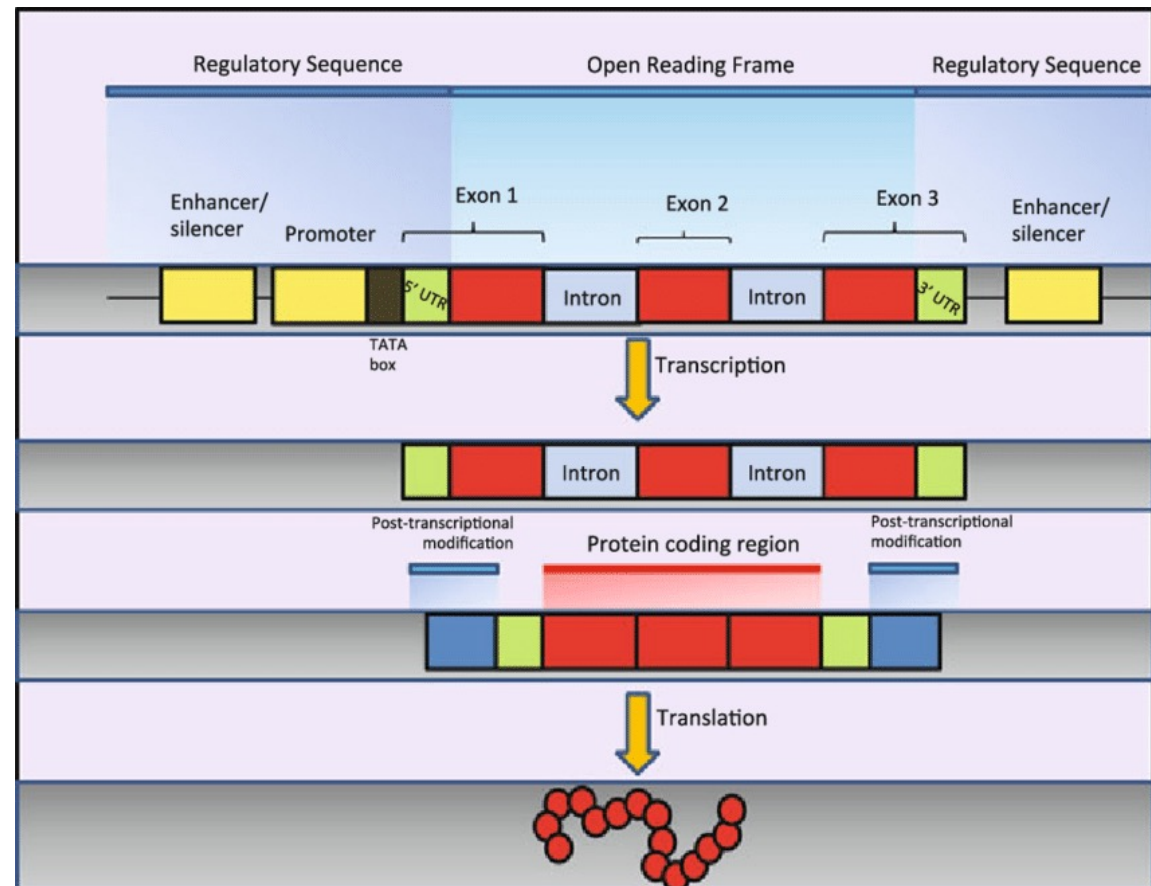
The Gene

Gene is a sequence of nucleotides in chromosomal DNA that encodes the synthesis of a gene product, either RNA or protein. Our chromosomes carry around 30000 genes



Protein coding genes are around 1% of DNA!

Basic structure of a gene



Genes does not encode only for proteins...

Genes encode for the synthesis of a gene product (functional unit), either RNA or protein as final result

Main Gene categories:

1. **Protein coding genes**, transcribed in mRNA, that encode for a specific protein. Up to 80% of the human genome might be involved in gene regulation, whereas only ~2% of the genome seems to code for proteins. The Human Genome Project, estimated that humans have between 20,000 and 25,000 protein coding genes.
2. **Ribosomal RNA genes**: transcribed in rRNA. They associate with ribosomal proteins to form ribosomes.
3. **Transfer RNA genes**, transcribed in tRNA. tRNA bind to specific amino acid and are responsible of translation of the genetic code from mRNA nucleotides to the amino acid sequence
4. Genes for Long non coding RNA (LncRNA)
5. Genes for MicroRNA (miRNA), that regulate mRNA stability
6. Genes for ribozymes, RNA molecules that have the ability to catalyze specific biochemical reactions, including RNA splicing

Table 14.2 Types of RNA

Type of RNA	Functions in	Function
Messenger RNA (mRNA) 	Nucleus, migrates to ribosomes in cytoplasm	Carries DNA sequence information to ribosomes
Transfer RNA (tRNA) 	Cytoplasm	Provides linkage between mRNA and amino acids; transfers amino acids to ribosomes
Ribosomal RNA (rRNA) 	Cytoplasm	Structural component of ribosomes



The human genome project



The Human Genome Project (HGP) was an international scientific research project with the goal of determining the base pairs that make up human DNA, and of identifying, mapping and sequencing all of the genes of the human genome from both a physical and a functional standpoint. It remains the world's largest collaborative biological project. Planning started after the idea was picked up in 1984 by the US government, the project formally launched in 1990, and was declared complete on April 14, 2003. Level "complete genome" was achieved in May 2021



...And today

← → ↻ [wired.com/story/whole-genome-sequencing-cost-200-dollars/](https://www.wired.com/story/whole-genome-sequencing-cost-200-dollars/) [Update](#)

≡ **WIRED** BACKCHANNEL BUSINESS CULTURE GEAR IDEAS SCIENCE SECURITY

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MEGAN MOLTENI

SCIENCE NOV 19, 2018 8:00 AM

Now You Can Sequence Your Whole Genome for Just \$200

Veritas is offering DNA reading, cheap, for two days. But most consumers don't understand the difference between that and a 23andMe test.



Comparative Genomics

NHGRI FACT SHEETS
genome.gov

Researchers choose the appropriate time-scale of evolutionary conservation for the question being addressed.

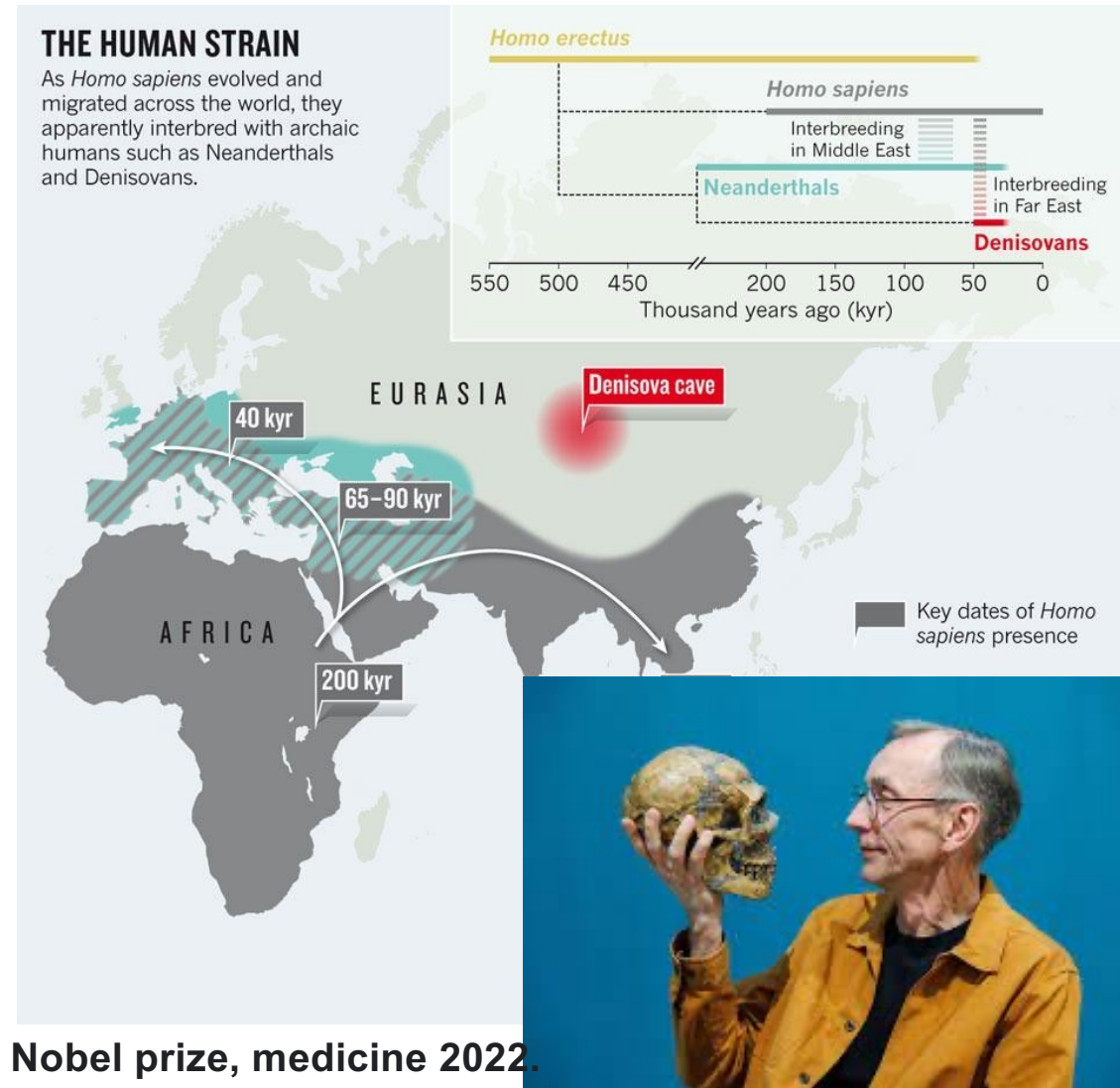
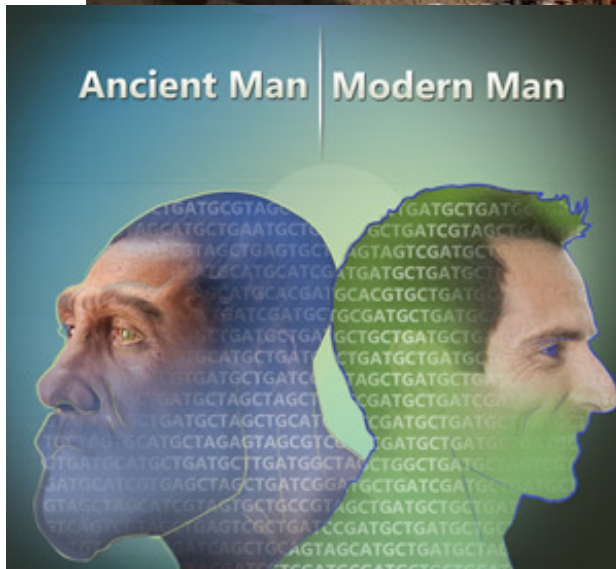
Common features of different organisms such as humans and fish are often encoded within the DNA evolutionarily conserved between them.

Looking at **closely related species** such as humans and chimpanzees shows which genomic elements are unique to each.

Genetic differences **within one species** such as our own can reveal variants with a role in disease.



DNA tells our story

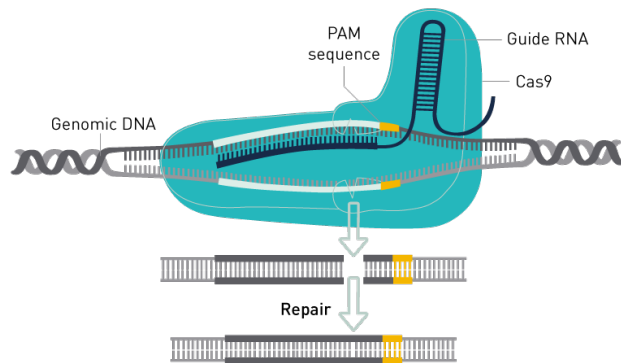


Svante Paabo, Nobel prize, medicine 2022.

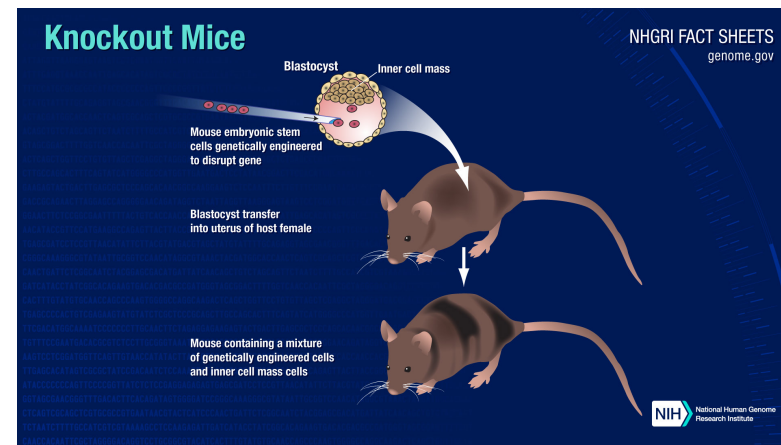


Exploring the genes functions!

Genetic engineering technologies applied to animal models helped to assess the individual genes functions. Today we can insert or delete single genes in animal models and study the health consequence of this modification. This will help us to identify the role of the gene.



CRISP gene editing technique

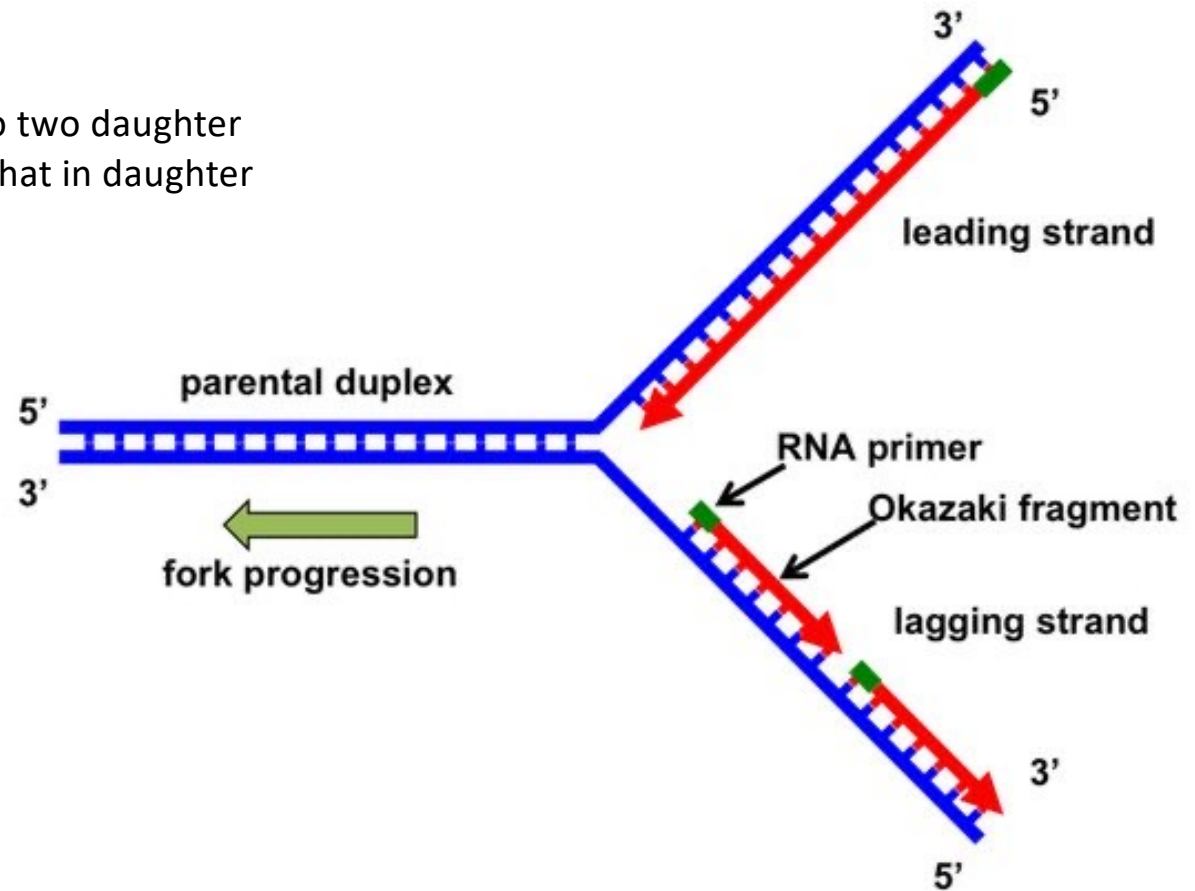


DNA replication

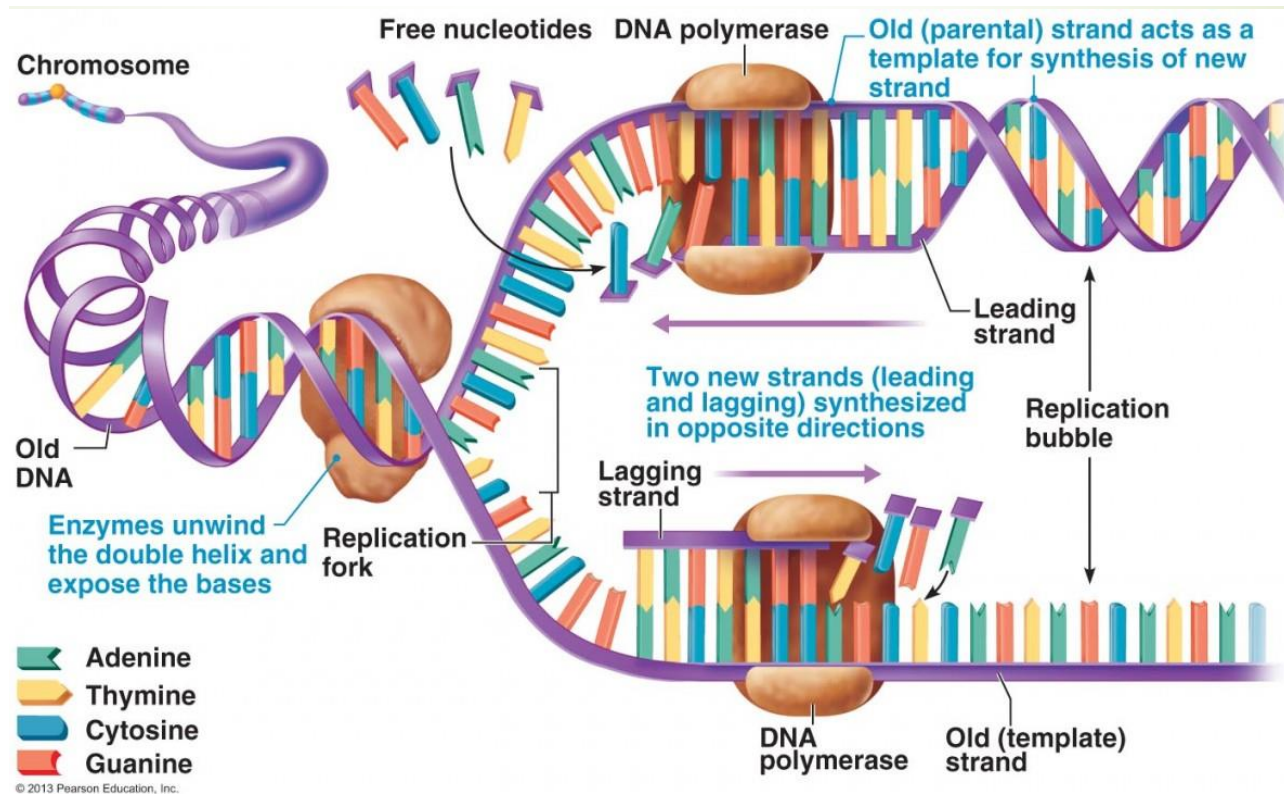
Before cell division, each DNA molecule replicates into two daughter molecules. Replication is semiconservative, meaning that in daughter molecules, one strand is conserved and one is new.

STEPS:

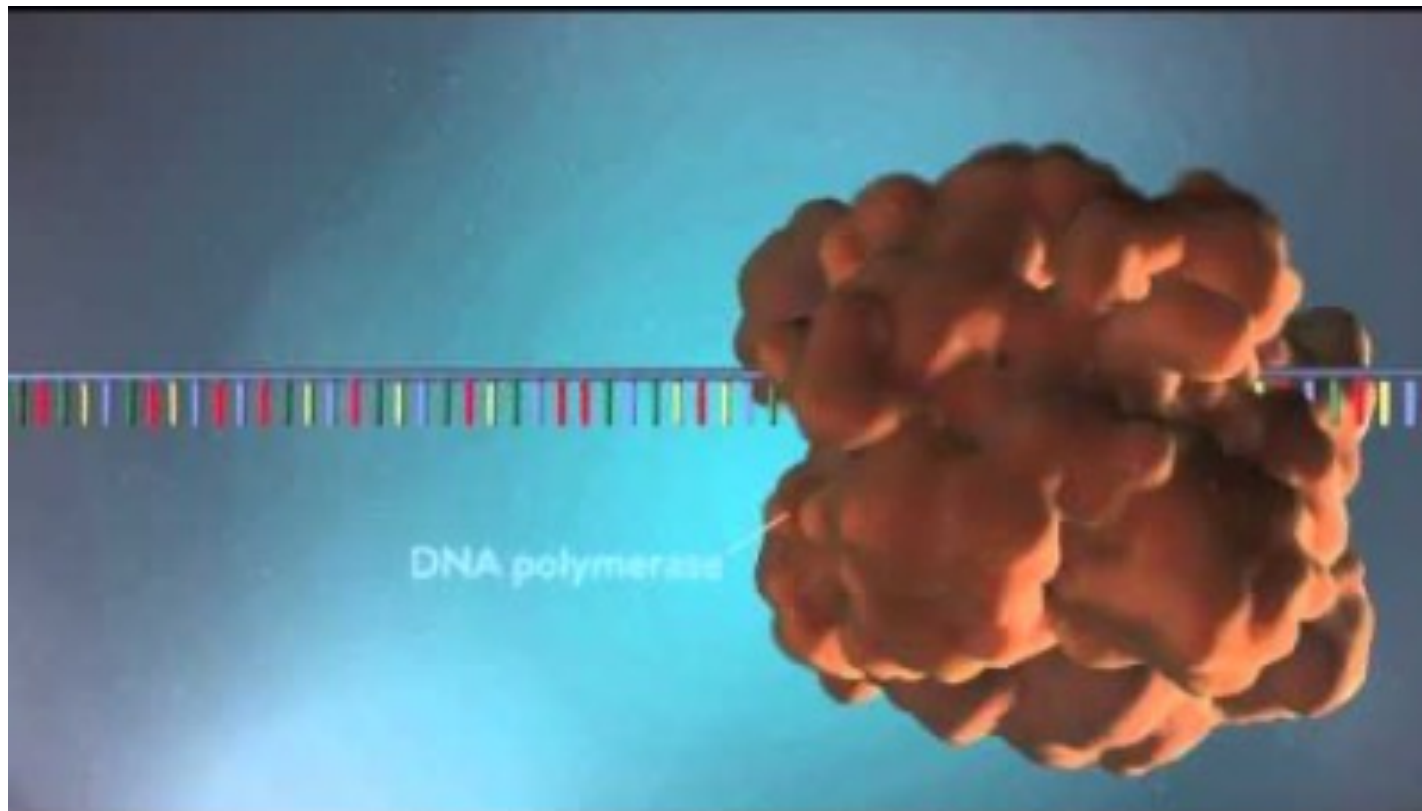
1. Denaturation and initiation of the replication fork at the ORI sites
2. Leading strand: formation of RNA primers by the **Primase enzyme**
3. **DNA polymerase** add nucleotides from the 5' to 3' direction continuously
4. Lagging strand: formation of many RNA primers
5. DNA polymerase add a short run of nucleotides from the 5' to 3' direction to form short chunks, the okazaki fragments
6. **Exonucleases** removes all the RNA primers from both strands and DNA polymerases fill the gap with DNA
7. **DNA ligase** seals up the fragments of DNA to form a continuous double strand



DNA replication



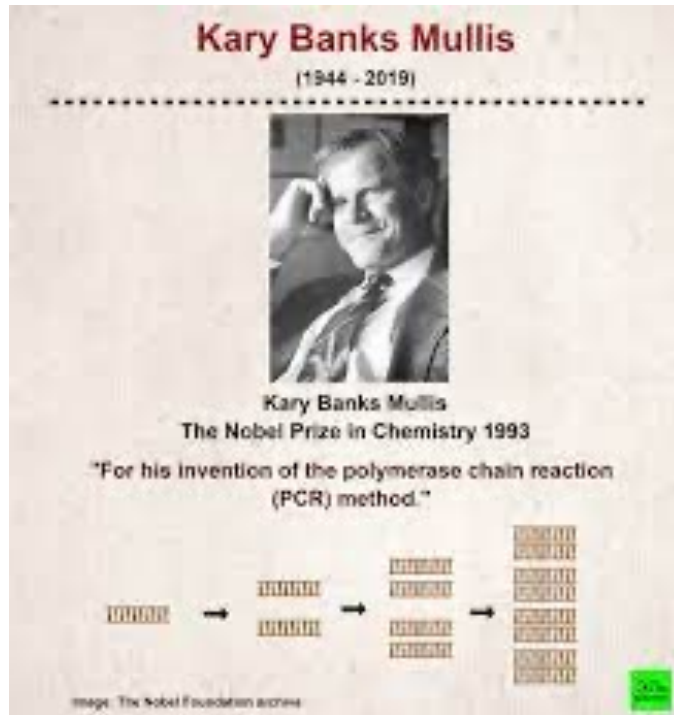
The replication of DNA



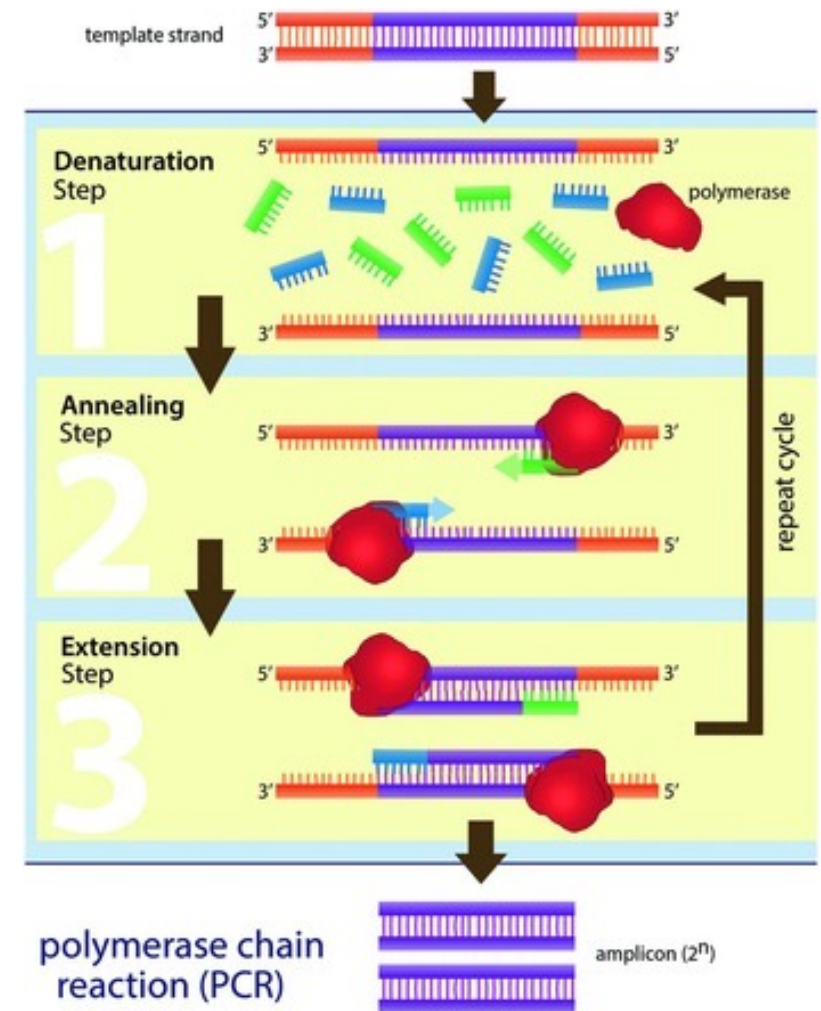
<https://www.youtube.com/watch?v=TNKWgcFPHqw>



Polymerase Chain Reaction (PCR)

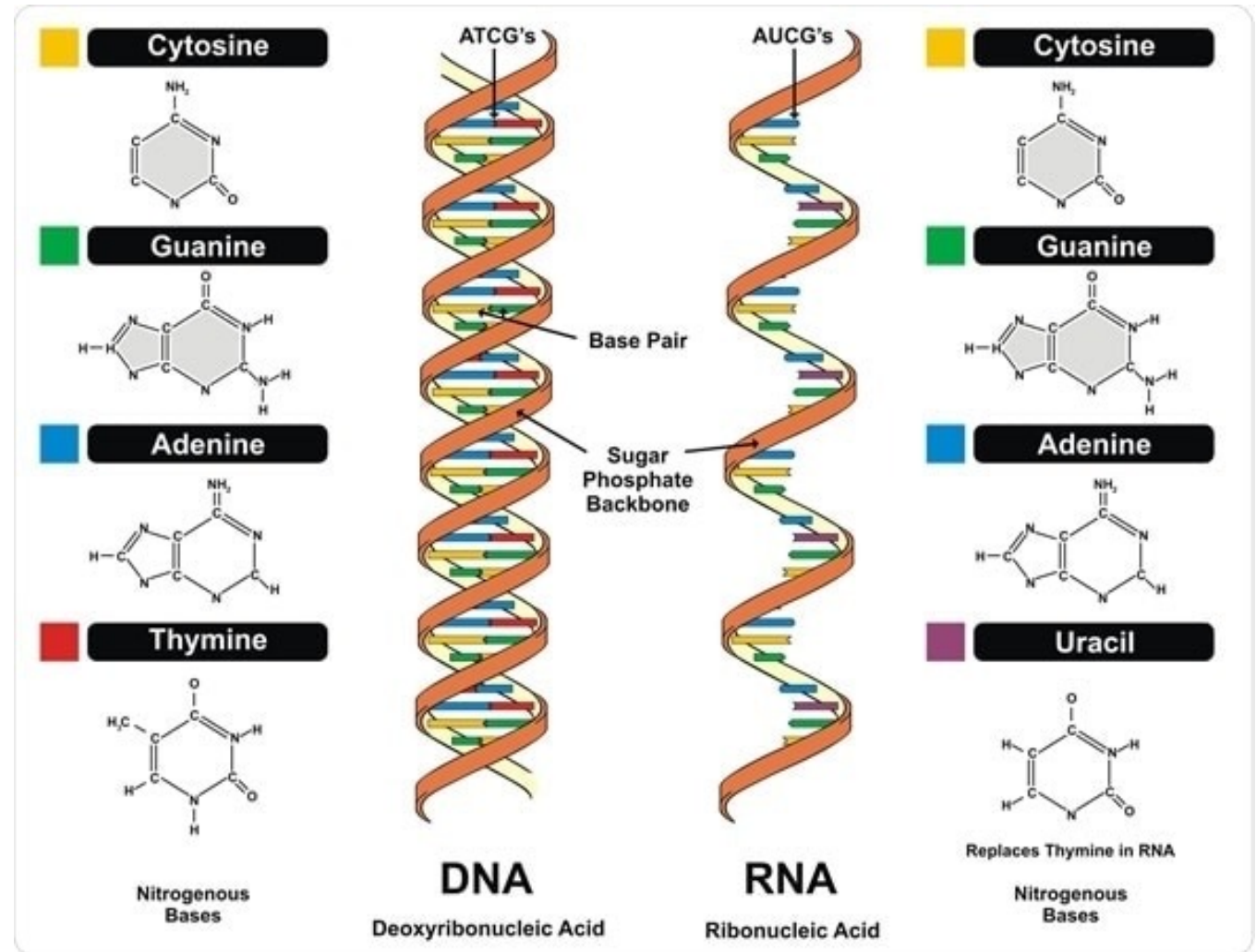


The activity of the DNA polymerase is exploited in the laboratory to obtain many copies of specific DNA sequences. The technique is called polymerase chain reaction, or PCR. With PCR, sufficient quantities of DNA are produced for chemical analysis or other manipulations, such as introducing DNA into cells.



RNA structure

- The Ribonucleic Acid (Rna) is a polynucleotide in **single filament**, composed of **Ribonucleotides** with **Uracile** instead of Thymine.



DNA vs. RNA

DNA

- deoxyribose sugar
- nitrogen bases
 - G, C, A, T
 - T : A
 - C : G
- double stranded



DNA

RNA

- ribose sugar
- nitrogen bases
 - G, C, A, U
 - U : A
 - C : G
- single stranded



RNA

The principal types of RNA at a glance

- Small non coding RNA (Transcriptional regulator)
- Rybozimes (Enzymatic activity, like splicing)

Table 14.2 Types of RNA		
Type of RNA	Functions in	Function
Messenger RNA (mRNA) 	Nucleus, migrates to ribosomes in cytoplasm	Carries DNA sequence information to ribosomes
Transfer RNA (tRNA) 	Cytoplasm	Provides linkage between mRNA and amino acids; transfers amino acids to ribosomes
Ribosomal RNA (rRNA) 	Cytoplasm	Structural component of ribosomes

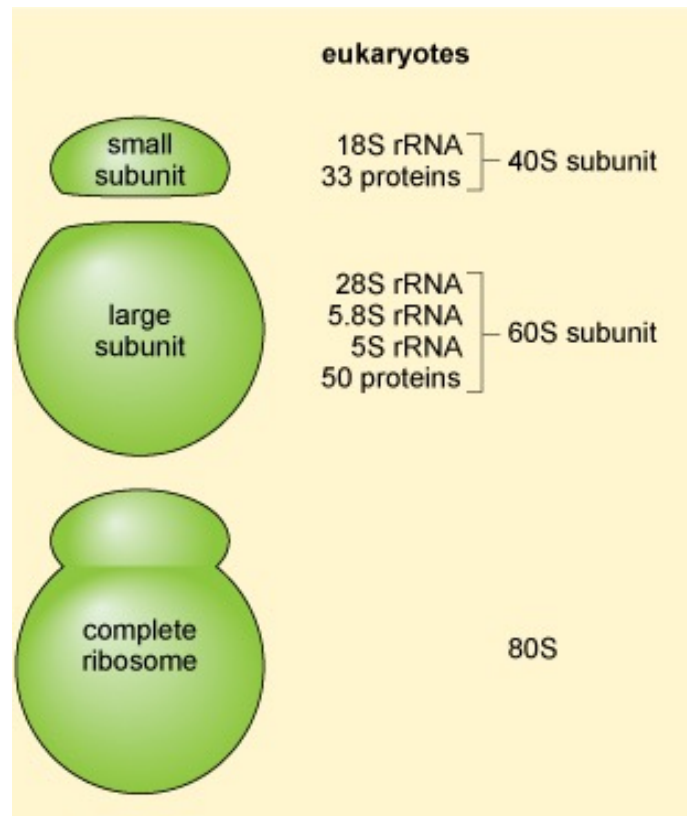
Messenger RNA (mRNA)



**RNA messaggero
(m-RNA)**

single-stranded linear molecule of RNA that corresponds to the genetic sequence of a gene and is read by a ribosome in the process of synthesizing a protein.

Ribosomal RNA



- Ribosomes are big ribonucleoprotein complexes
- rRNA is contained in ribosomes.
- 4 rRNA fragments are associated with proteins to form the two subunits in ribosomes

tRNA structure

- The RNA filament is shorter than the DNA ones, and can fold in different shapes (eg Hairpin) due to palindromic sequences

