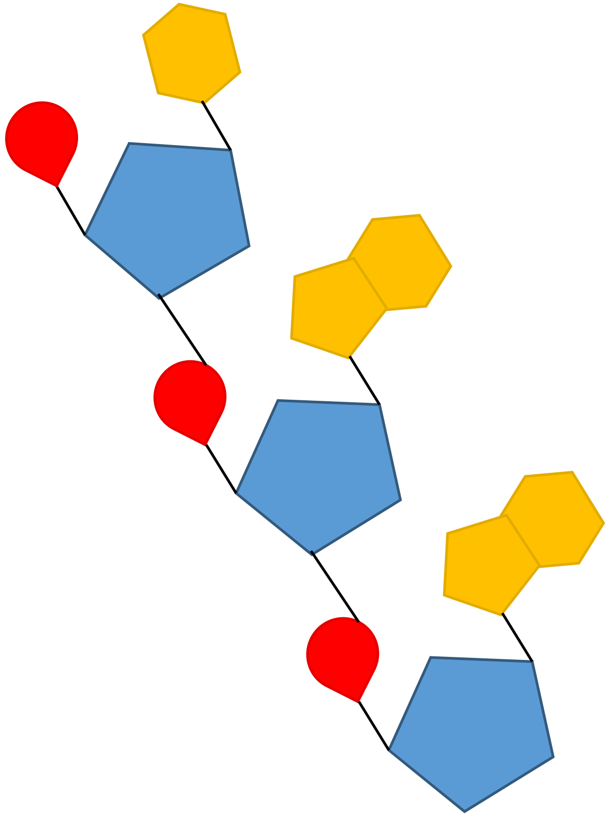
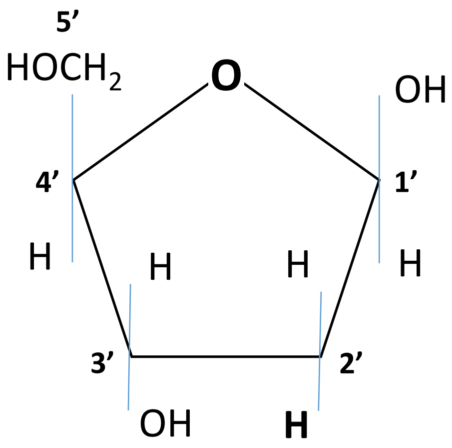
Nature, structure and spatial organization of hereditary material



Rafael Navajas-Pérez
www.rafaelnavajas.eu

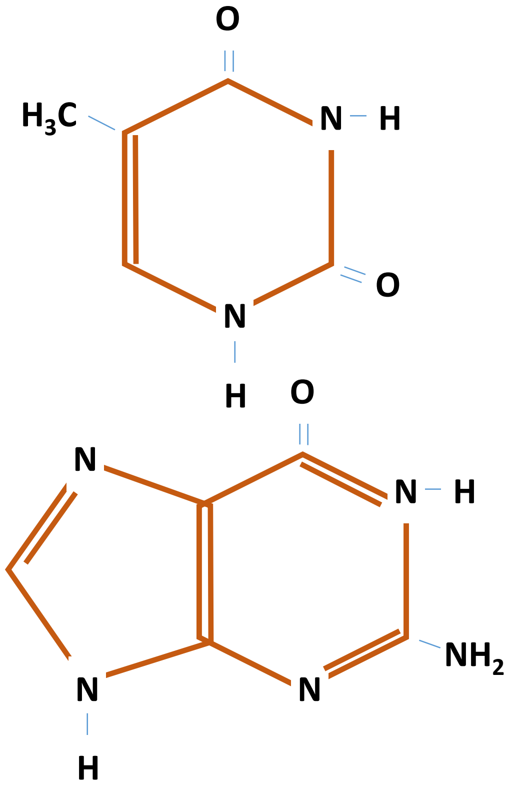
UNIVERSIDAD DE GRANADA

DNA composition

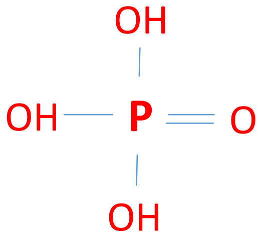


Pentose

(Deoxyribose)

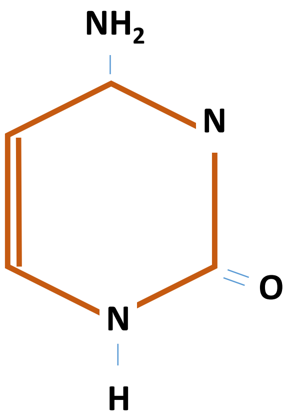


Nucleobase

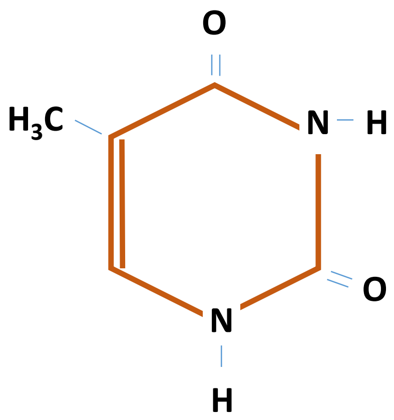


Phosphoric acid

DNA nucleobases



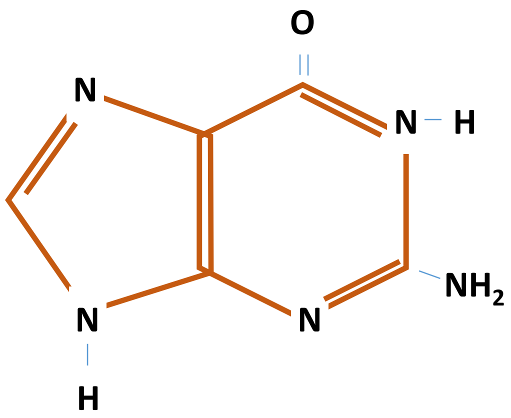
Cytosine



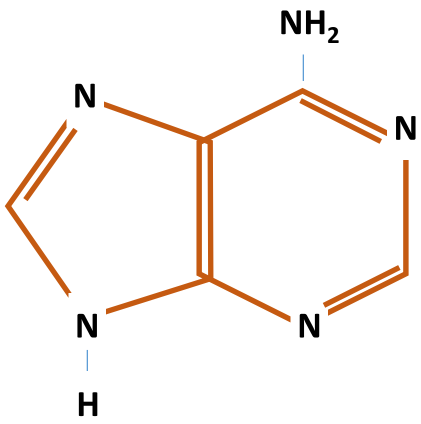
Thymine

PYRIMIDINES

PURINES

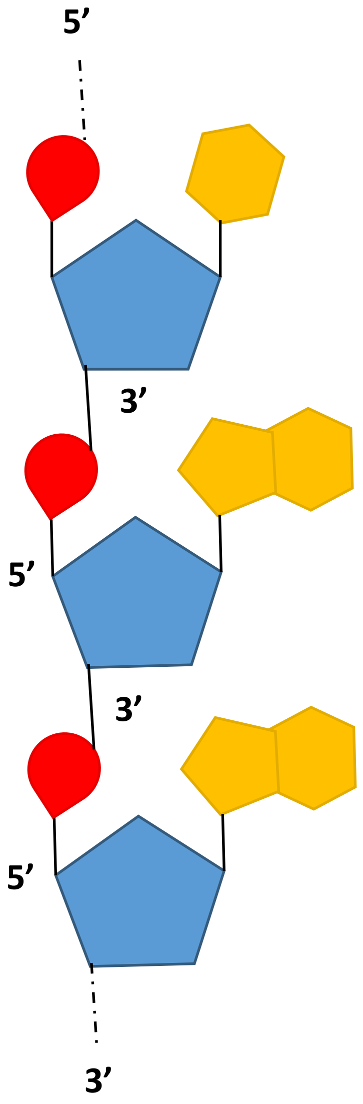


Guanine



Adenine

DNA primary structue: chain of nucleotides with phosphodiester bonds.



CHARGAFF RULES: to explain the proportion of different nucleobases in **<u>double-helix DNA.</u>**

1.- A=T: the number of Adenines equals the number of Thymines.

2.- C=G: the number of Cytosines equals the number of Guanines.

3.- Purines=pyrimidines: *purines* (Adenine + Guanine) = *pyrimidines* (Thymine + Citosine).

ACGTTTTCCGACGATCTAAA

TGCAAAAGGCTGCTAGATTT

TTCCGTTTTCCGACTTCGCT

AAGGCAAAAGGCTGAAGCGA

ACGTTTTCCGACGATCTAAA

TGCAAAAGGCTGCTAGATTT

A/T = 12/12

C/G = 8/8

(A+G) = (T+C) = 20

TTCCGTTTTCCGACTTCGCT

AAGGCAAAAGGCTGAAGCGA

A/T = 10/10

C/G = 10/10

(A+G) = (T+C) = 20

CHARGAFF RULES: to explain the proportion of different nucleobases in **double-helix DNA.**

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There is a purine for each pyrimidin, and they appear coupled

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There is a purine for each pyrimidin, and they appear coupled

4.- (A+T)/(C+G): Adenine & Thymine and Cytosine & Guanine proportion is variable and depends on the species considered.

ACGTTTTCCGACGATCTAAA
TGCAAAAGGCTGCTAGATTT

A/T = 12/12

C/G = 8/8

(A+T)/(C+G) = 24/16

TTCCGTTTTCCGACTTCGCT
AAGGCAAAAGGCTGAAGCGA

A/T = 10/10

C/G = 10/10

(A+T)/(C+G) = 20/20

CHARGAFF RULES: to explain the proportion of different nucleobases in **double-helix DNA.**

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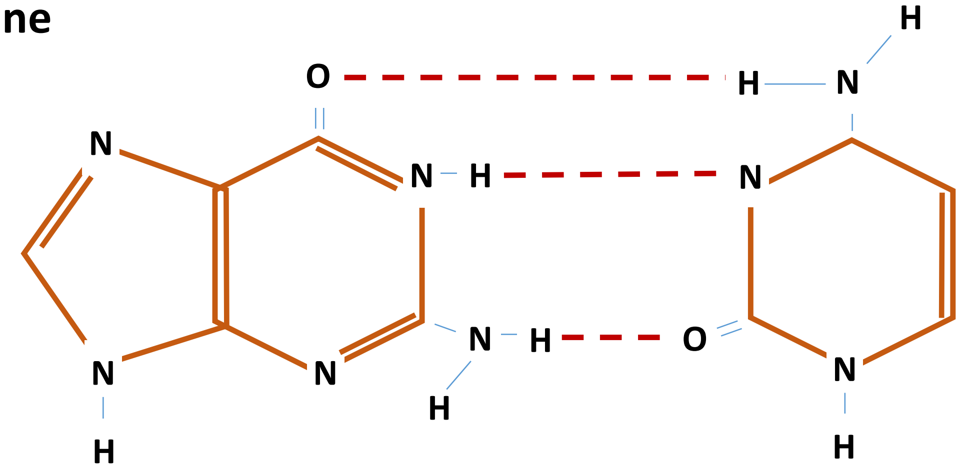
There is a purine for each pyrimidin, and they appear coupled

4.- (A+T)/(C+G): Adenine & Thymine and Cytosine & Guanine proportion is variable and depends on the species considered.

DNA molecules differ in nucleobases composition

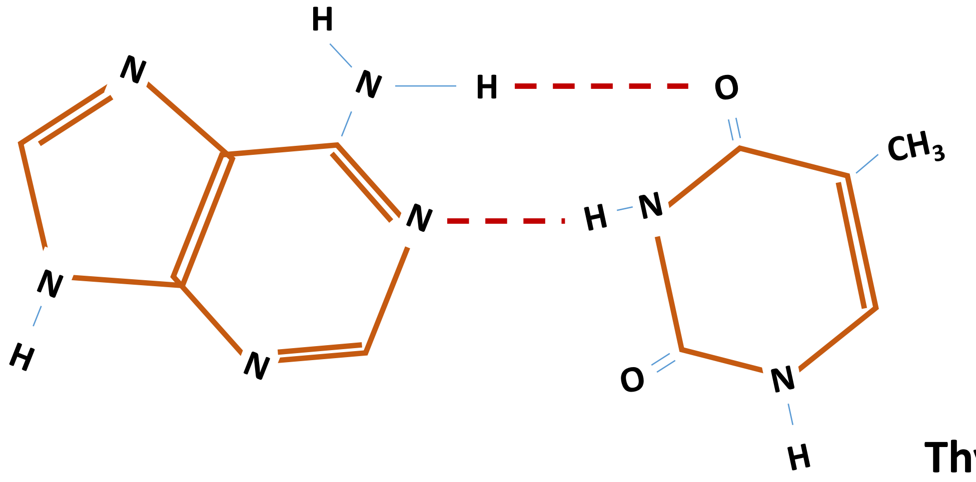
Complementarity

Guanine

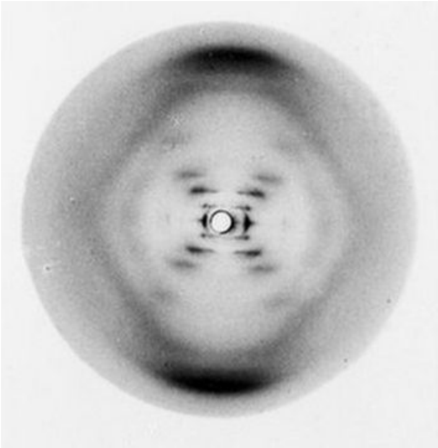


Cytosine

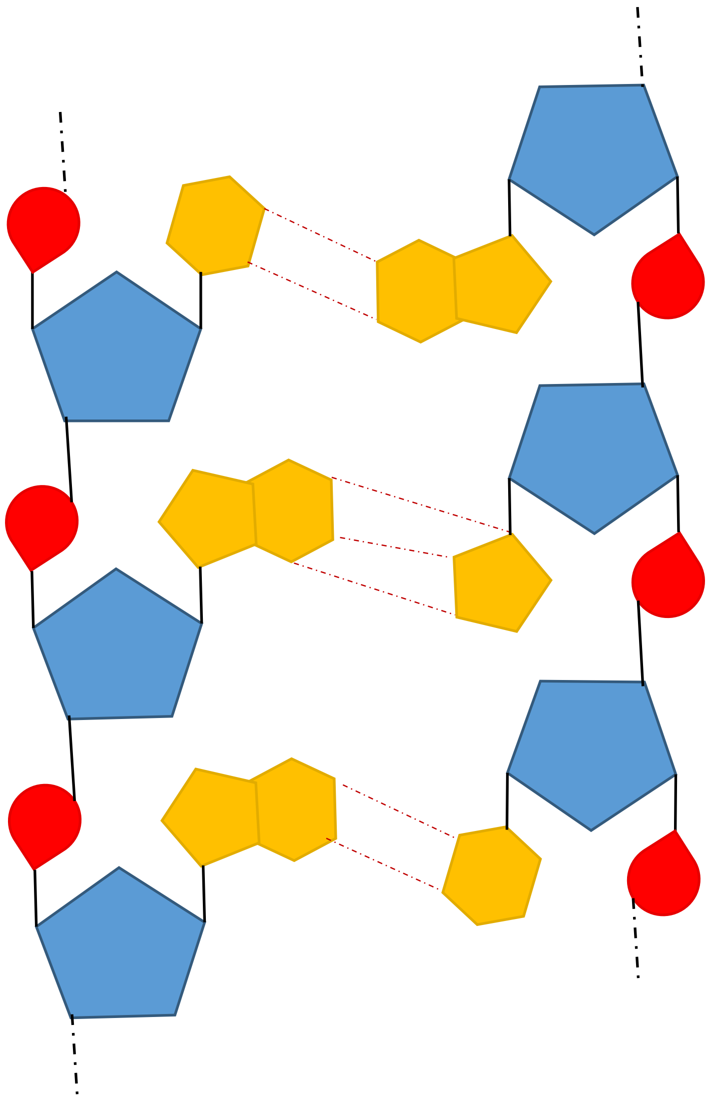
Adenine



Thymine



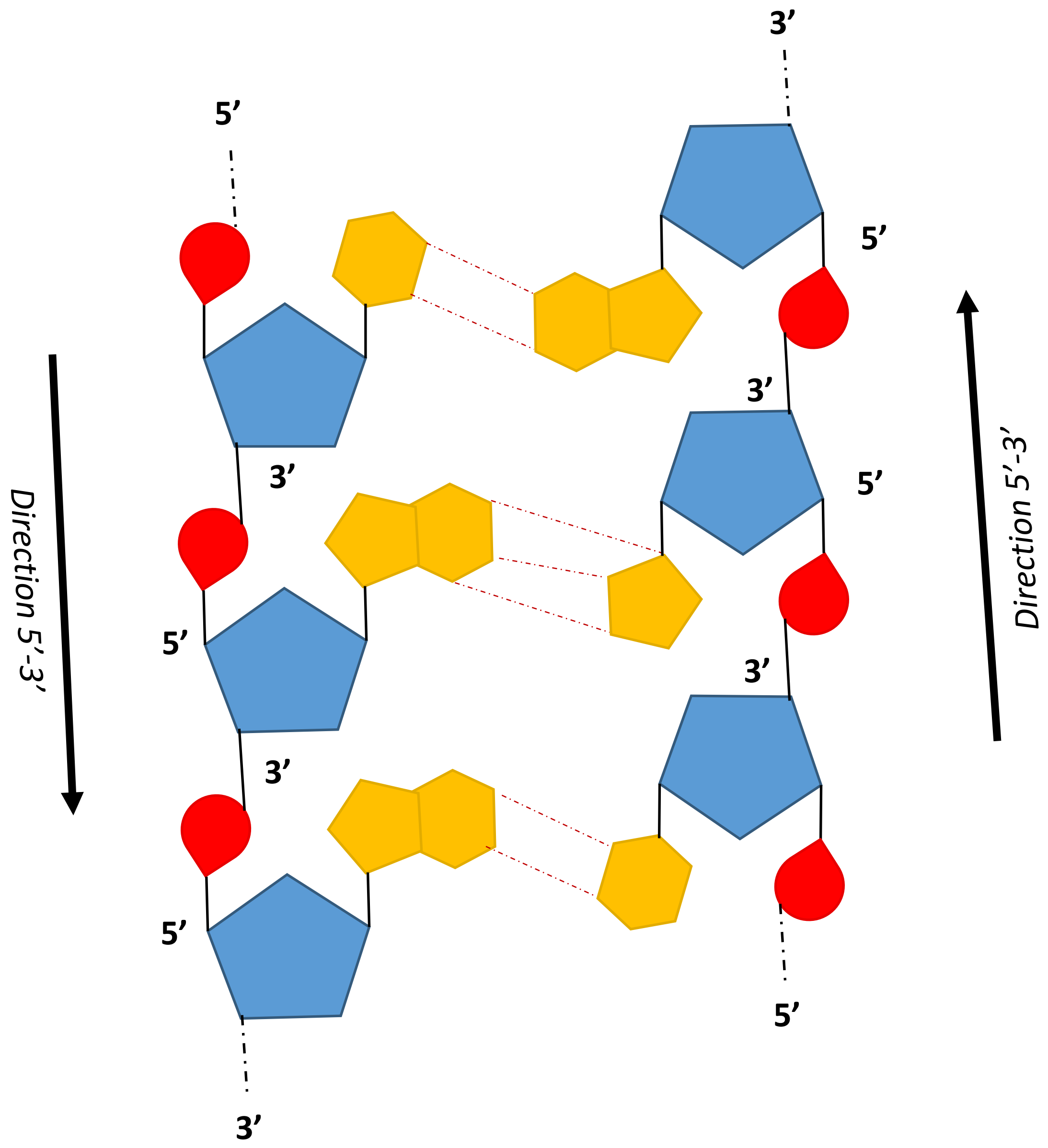
DNA secondary structure: chains are antiparallel and complementary.



5’ ACGTTTTCCGACGATCTAAA 3’

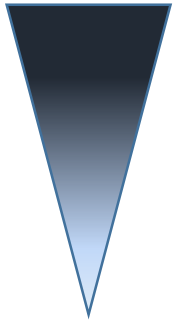
3’ TGCAAAAGGCTGCTAGATTT 5’

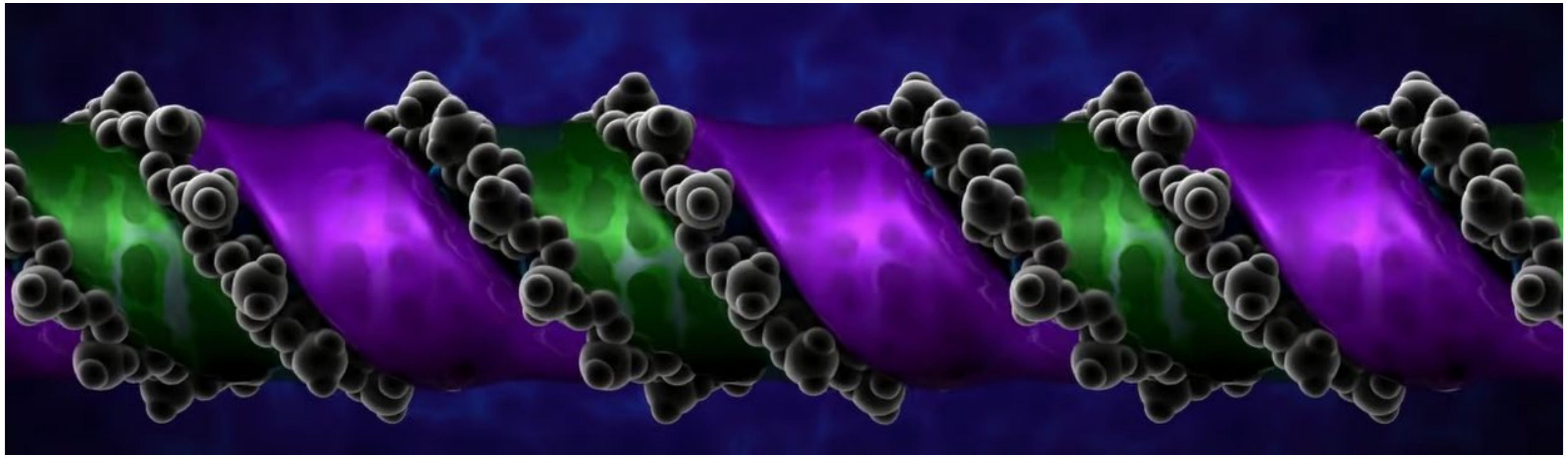
DNA secondary structure: chains are antiparallel and complementary.



TYPES OF BONDS:

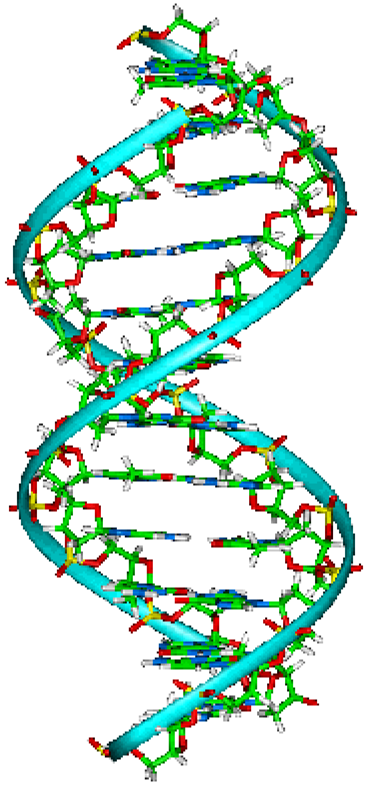
- Phosphodiester (1ª)
- H bond(2ª)
- Pi-stacking (2ª)



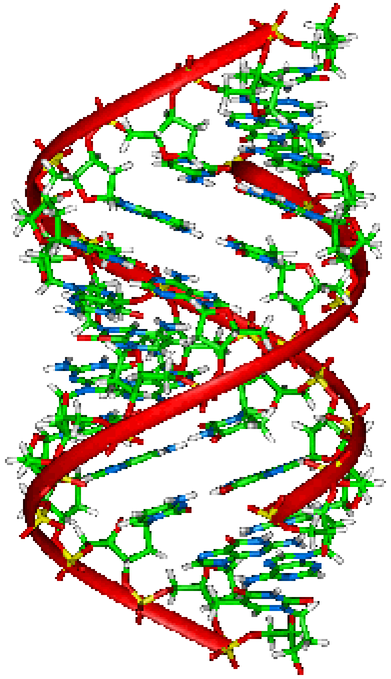


Source: MITx Bio

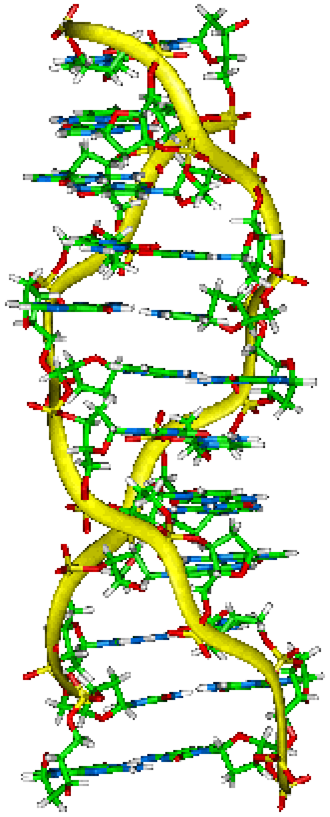
DNA secondary structure: chains are antiparallel and complementary.
Stable 3D structure.



DNA-B



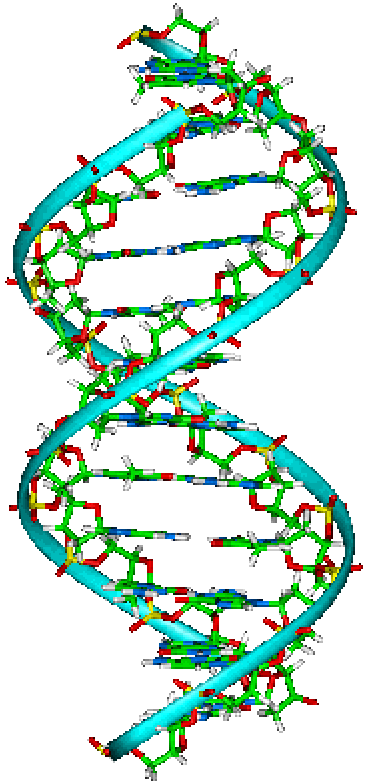
DNA-A



DNA-Z

Source: Wikipedia

DNA secondary structure: chains are antiparallel and complementary.
Stable 3D structure.

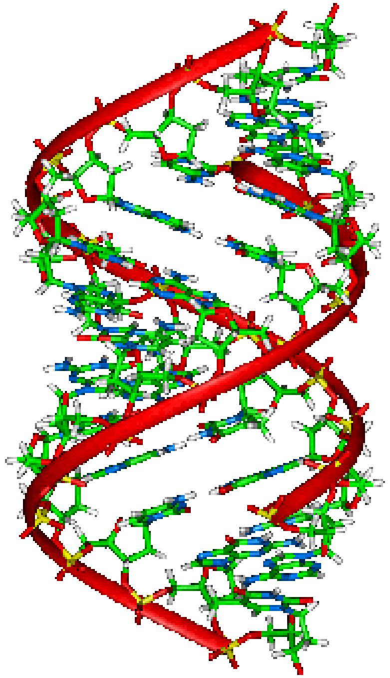


DNA-B

Particulars	B DNA
Helix	Right handed
Base pairs per turn	~10.5
Helical Diameter (nm)	2.0
Helical length (nm)	3.4
Shape	Intermediate
Major Grove	Narrow, deep
Minor Grove	Broad, shallow

B-DNA
92% H_2O

DNA secondary structure: chains are antiparallel and complementary.
Stable 3D structure.



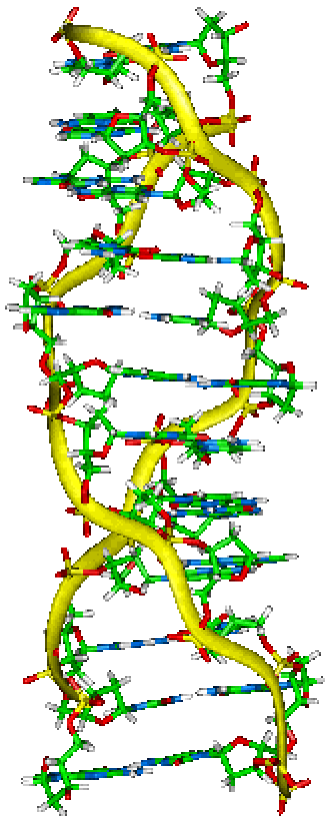
DNA-A

Particulars	A DNA
Helix	Right handed
Base pairs per turn	~11
Helical Diameter (nm)	2.6
Helical length (nm)	2.6
Shape	Broadest
Major Grove	Wide, deep
Minor Grove	Narrow, shallow

A-DNA

75% H_2O

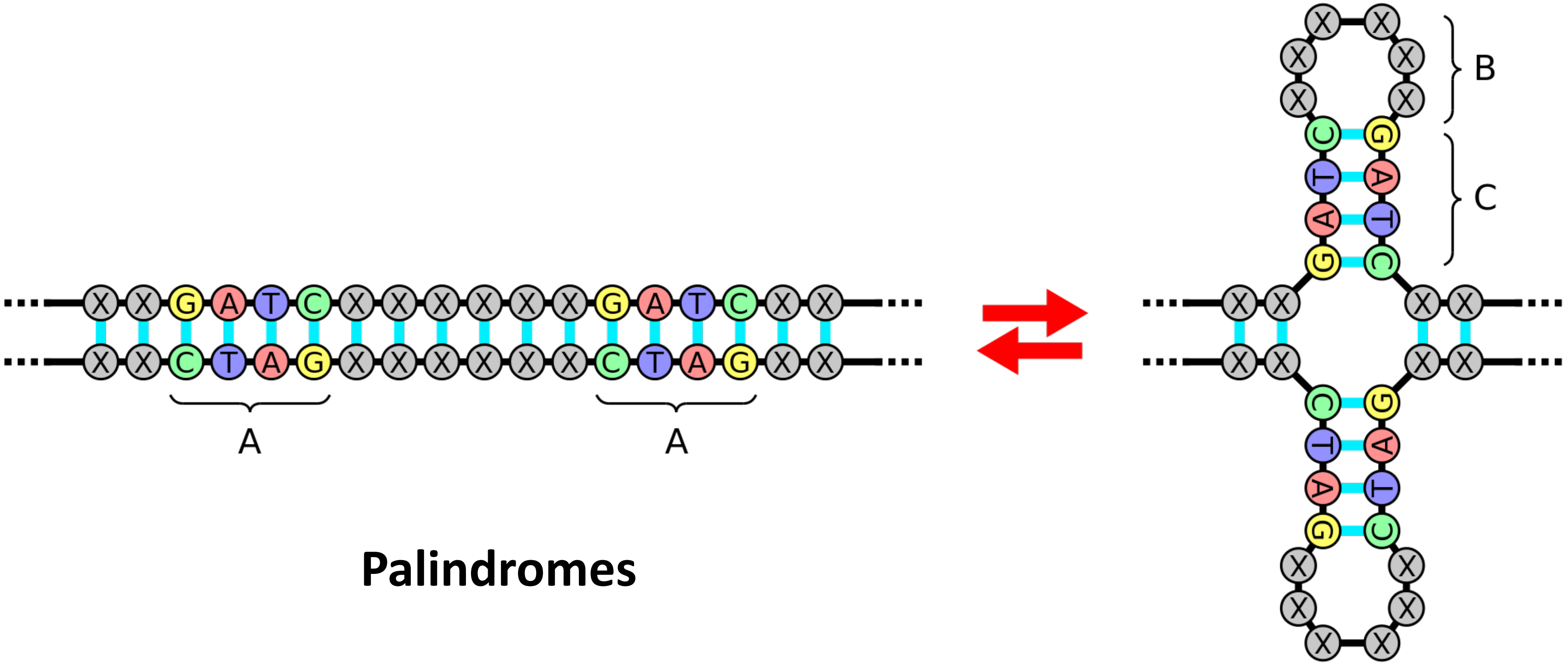
DNA secondary structure: chains are antiparallel and complementary.
Stable 3D structure.



DNA-Z

Particulars	Z DNA
Helix	Left handed
Base pairs per turn	~12
Helical Diameter (nm)	1.8
Helical length (nm)	3.7
Shape	Narrowest
Major Grove	Flat
Minor Grove	Narrow, deep

DNA secondary structure: chains are antiparallel and complementary.
Stable 3D structure.



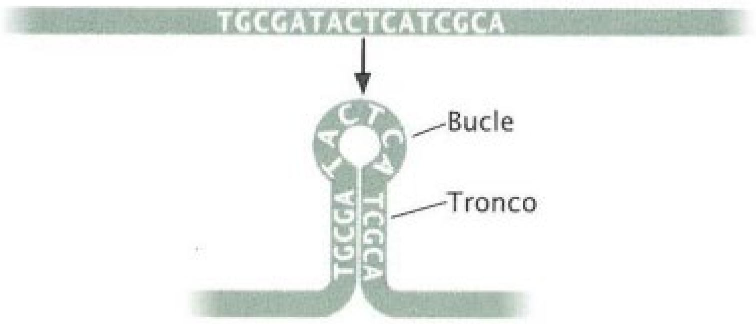
Palindromes

Source: Acdx., Wikipedia

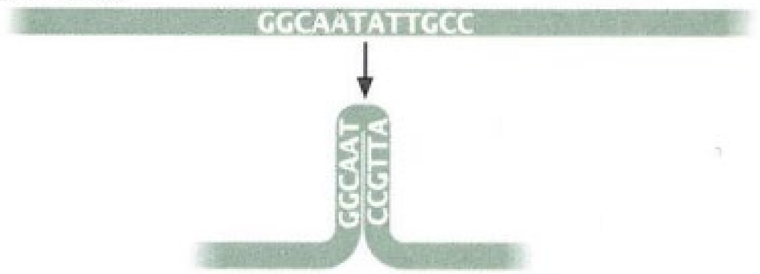
DNA secondary structure: chains are antiparallel and complementary.
Stable 3D structure.

Palindromes & Complementary Regions

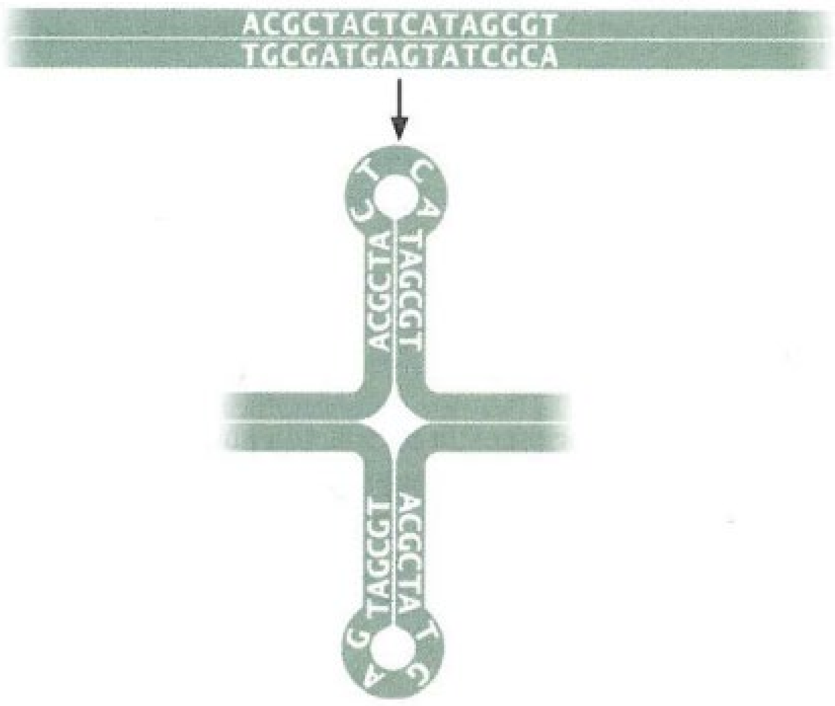
Loops



Forks

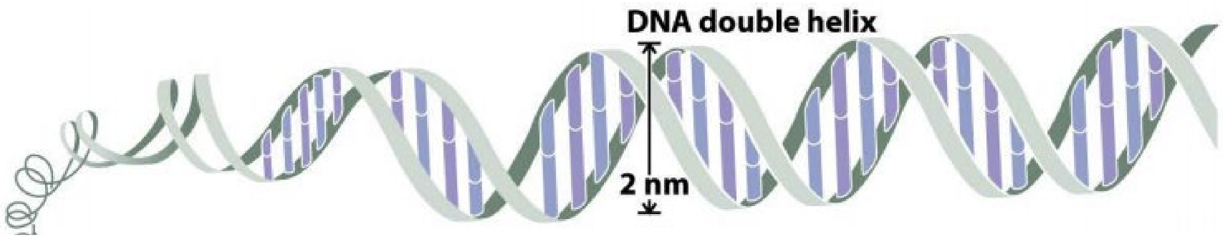


Cross



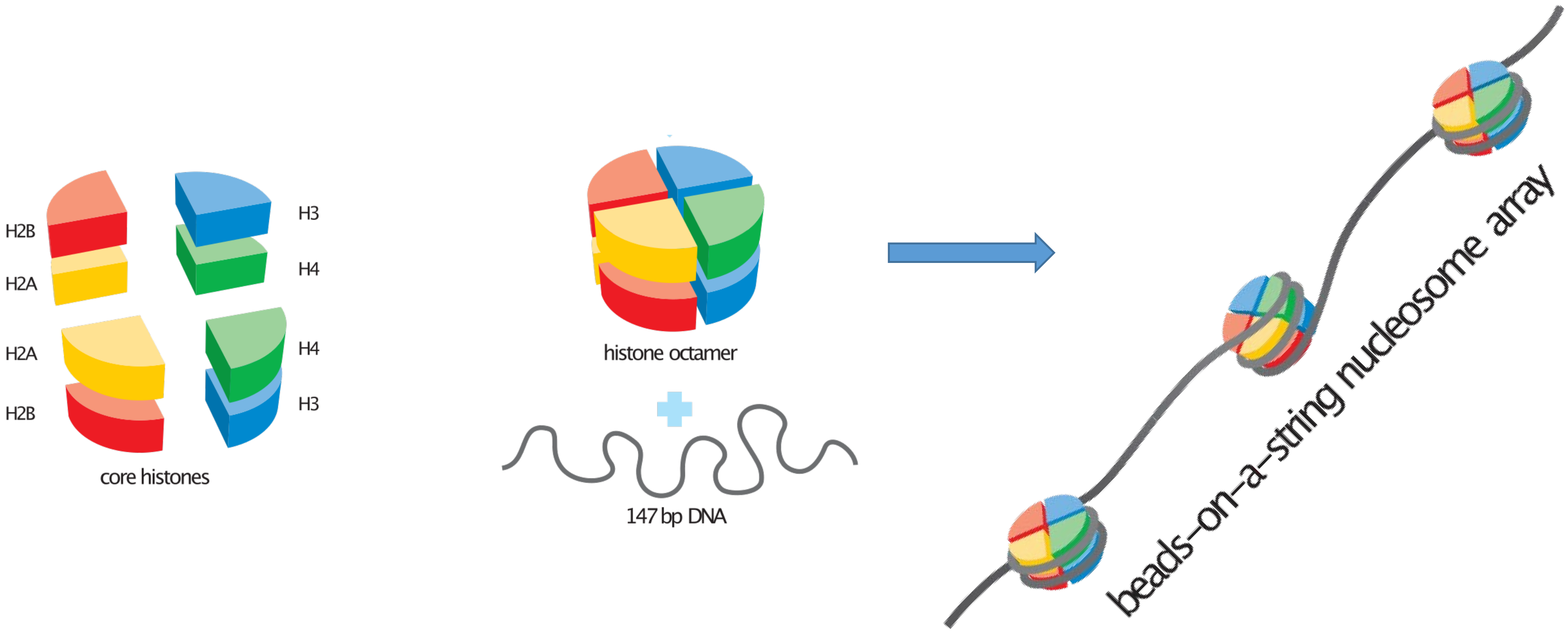
Source: Panamericana

DNA tertiary structure: DNA packaging and protein binding.



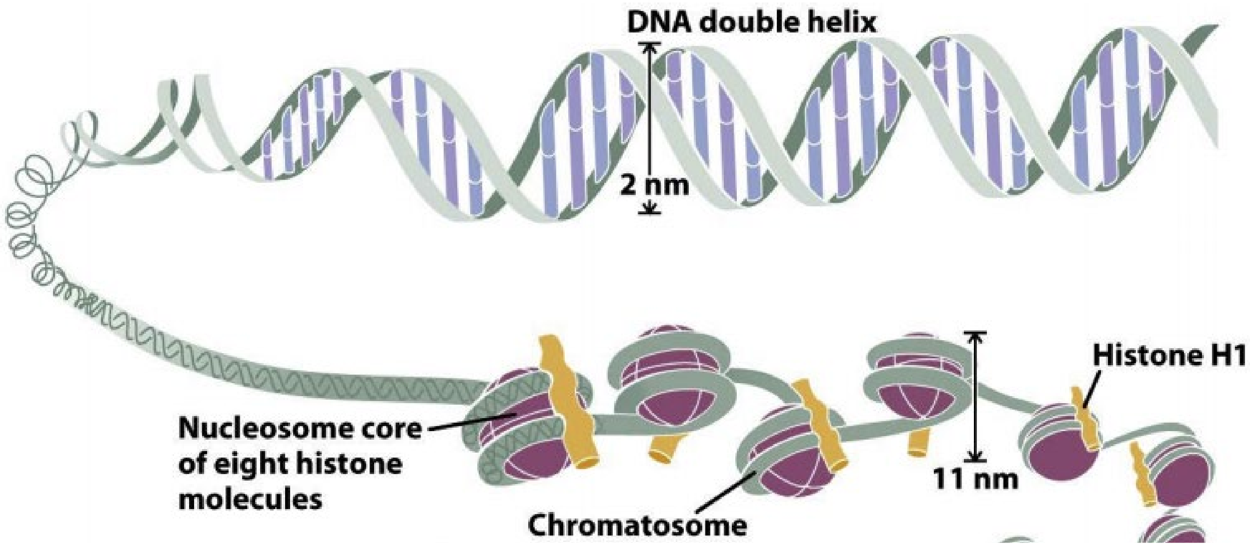
Source: Panamericana Ed.

Histone Octamer or Nucleosome

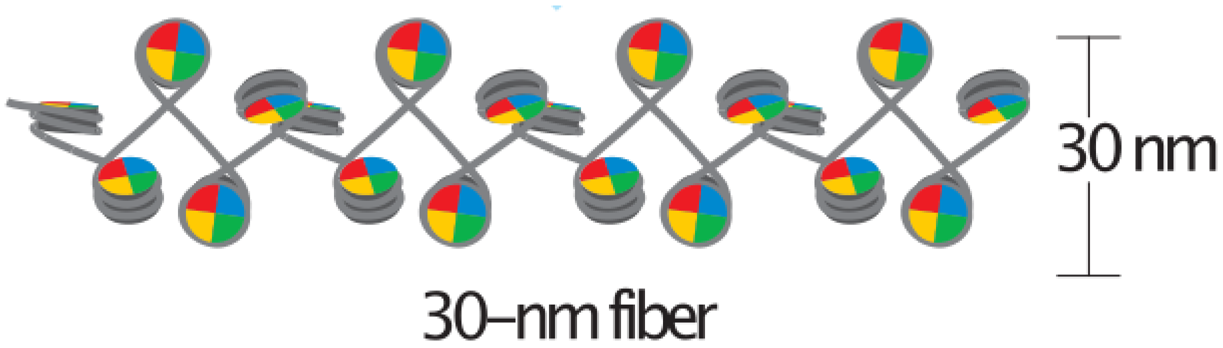


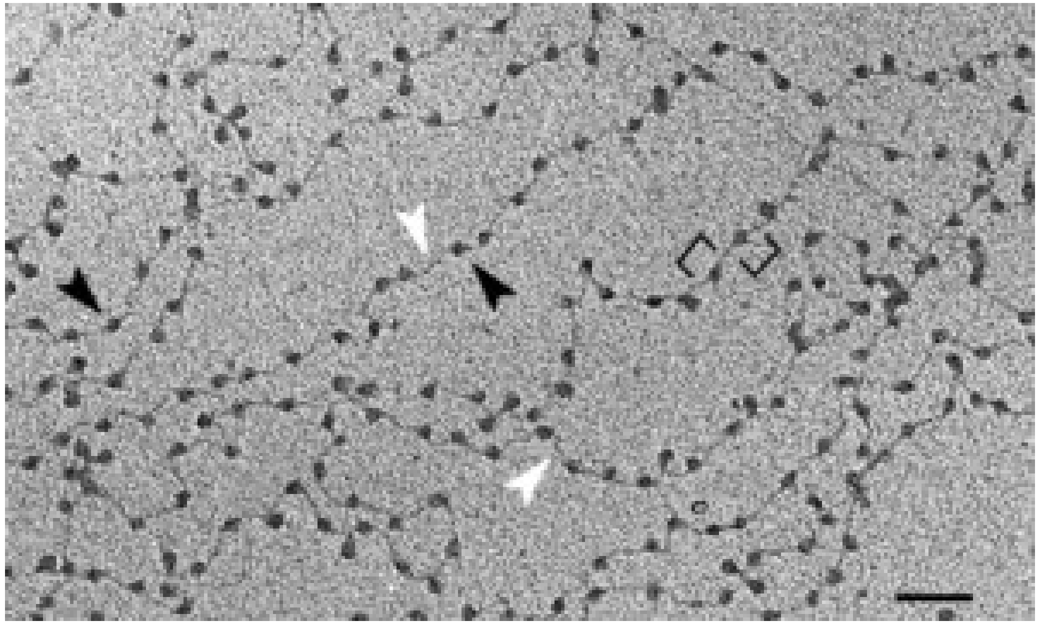
Source: Wikipedia

DNA tertiary structure: DNA packaging and protein binding.

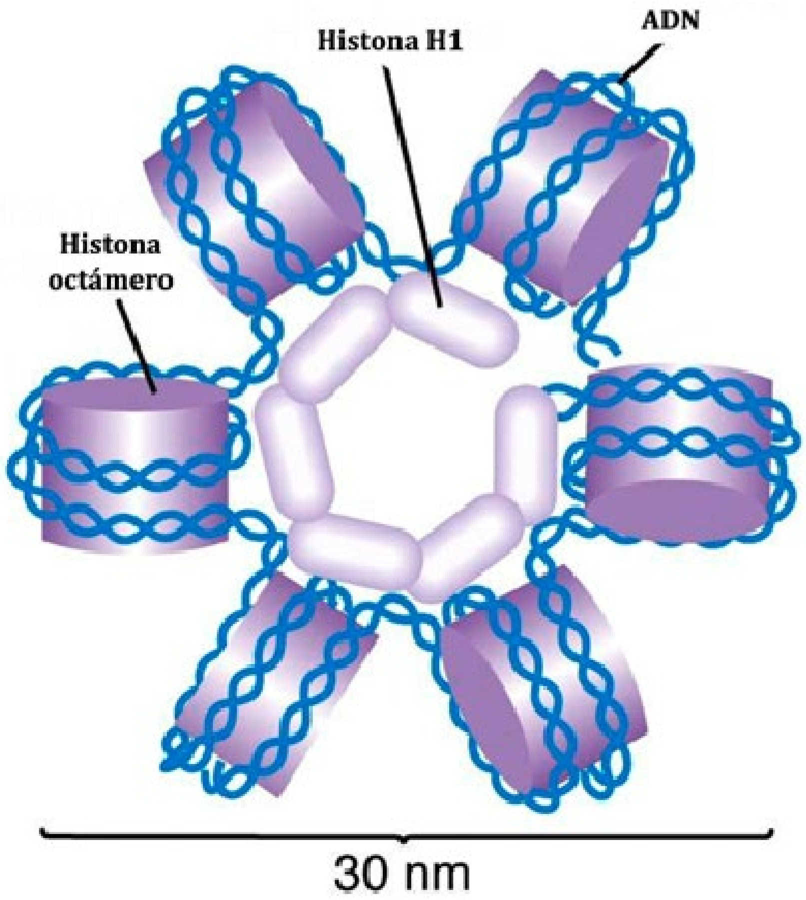


Fuente: Panamericana Ed.



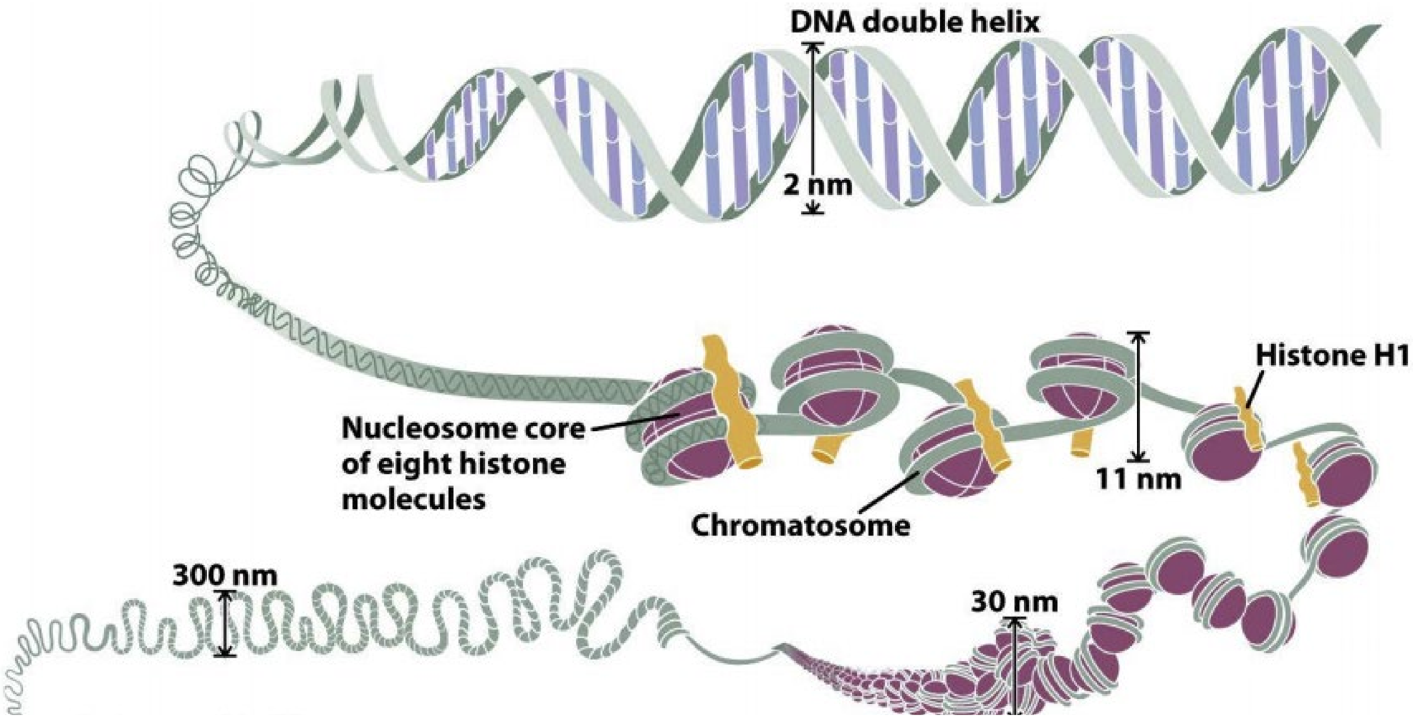


Beads on “string” structure



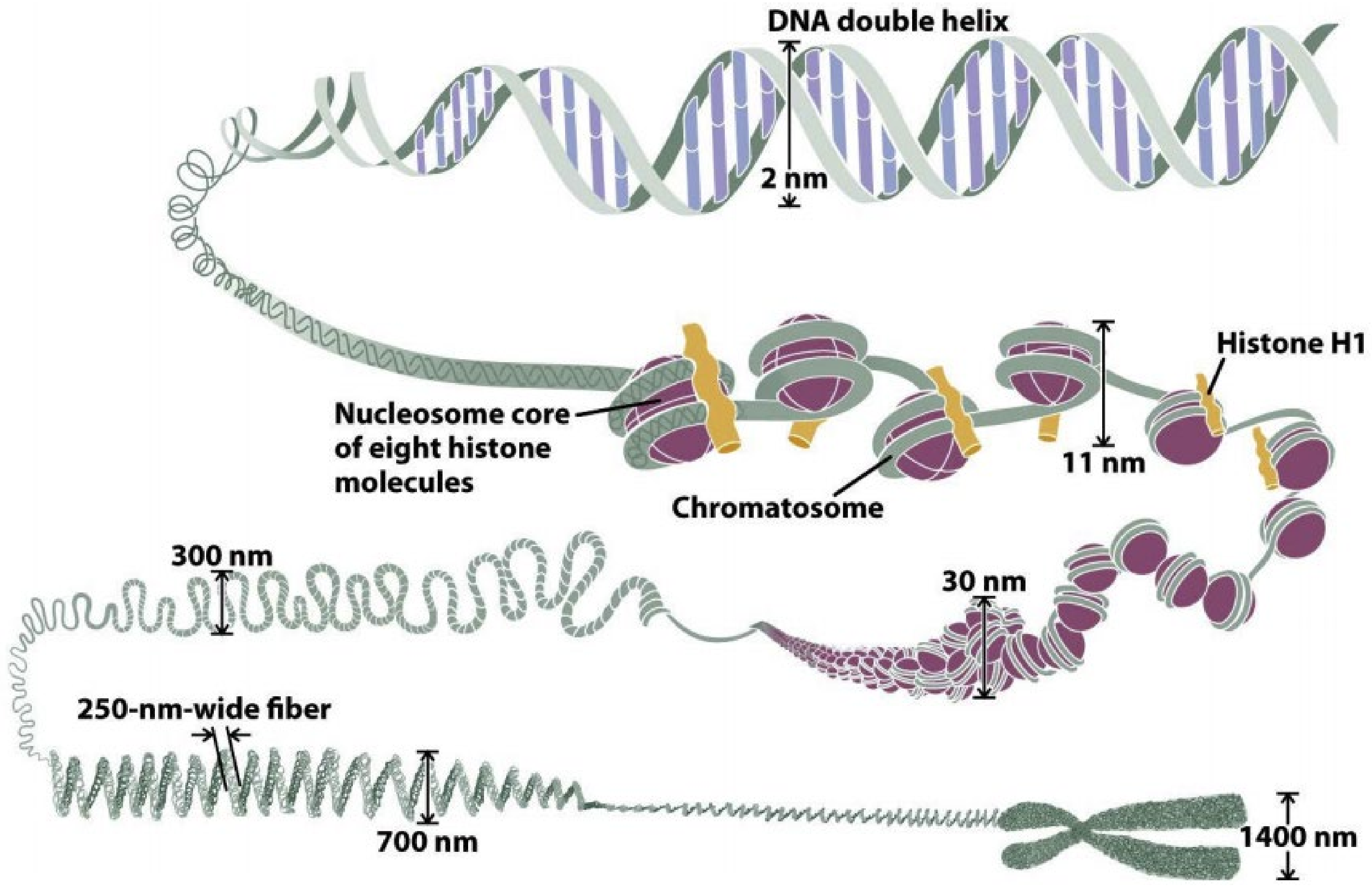
Source: Wikipedia and Info-Farmacia

DNA tertiary structure: DNA packaging and protein binding.



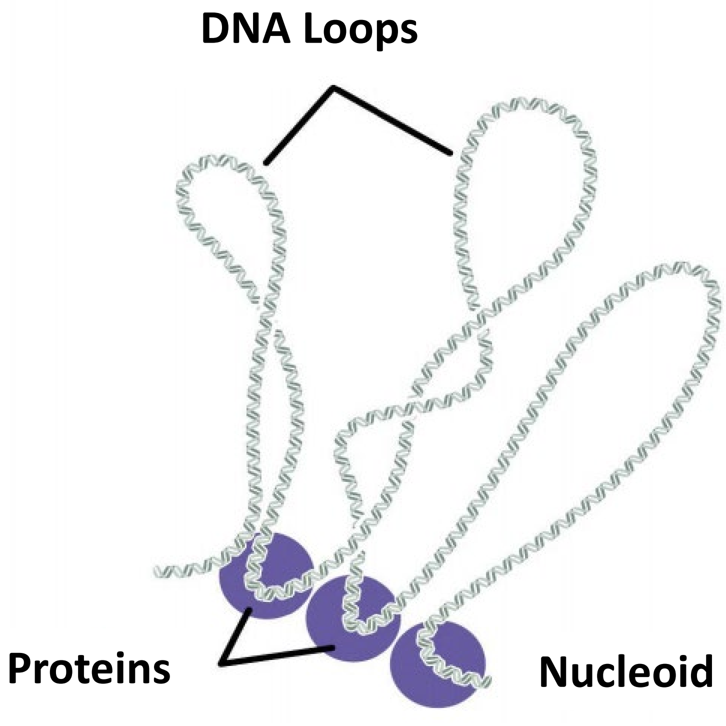
Source: Panamericana Ed.

DNA tertiary structure: DNA packaging and protein binding.

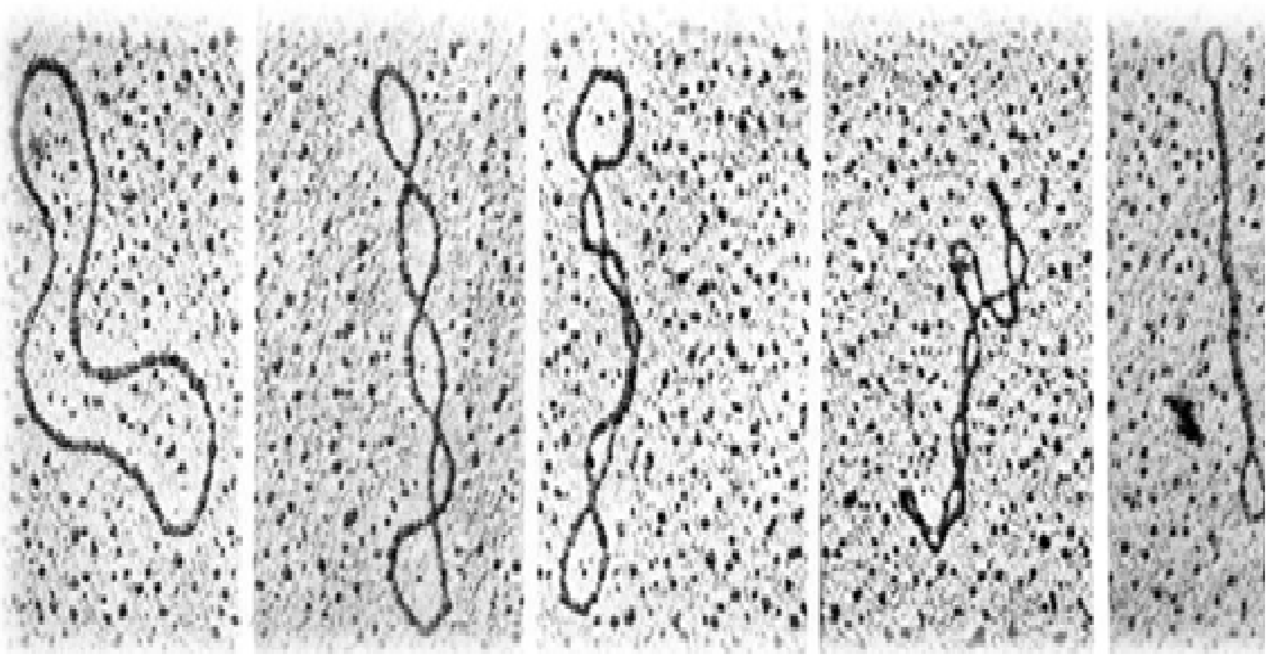


Source: Panamericana Ed.

DNA tertiary structure: DNA packaging and protein binding.



DNA SUPERCOILING IN BACTERIAL CHROMOSOMES:



Source: Panamericana

DNA tertiary structure: DNA packaging and protein binding.

POLYTENE CHROMOSOMES O CROMOSOMAS GIGANTES:

- In salivary glands, digestive tract and rectum of *Drosophila* larvae.
- Homologous chromosomes are paired (**although they belong to somatic cells**).
- Multiple DNA strands paired.
- Intensely stained regions and decondensed regions (*puffs*), these later indicate high rate of transcription.

Source: rafaelnavajas.eu

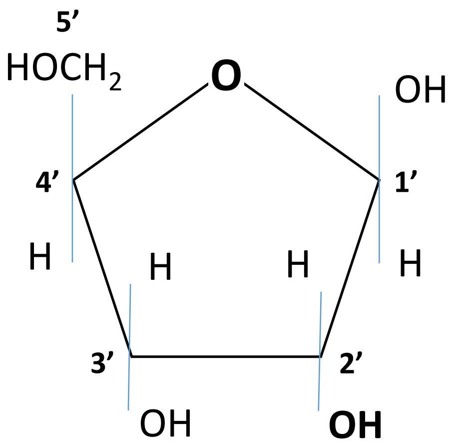
DNA tertiary structure: DNA packaging and protein binding.

LAMPBRUSH CHROMOSOMES:

- Oocites of sharks, salamanders and spermatocytes of many vertebrates.
- Meiotic chromosomes with regions of decondensed chromatin.
- Large size, especially in diplotene.
- These *loops* are probably made of RNA (indicating high rate of gene transcription).

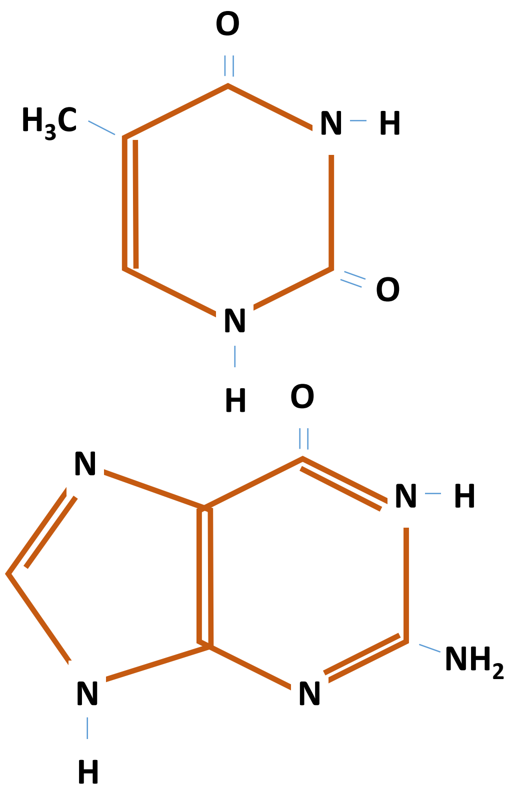
Source: Oskar Hertwig, Wikipedia

RNA composition

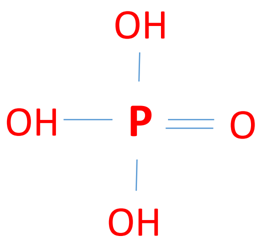


Pentose

(Ribose)



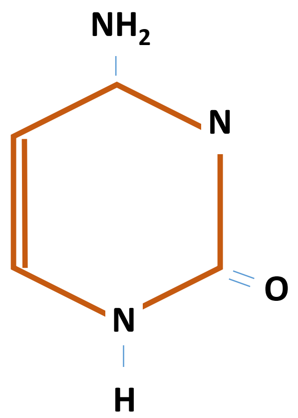
Nucleobase



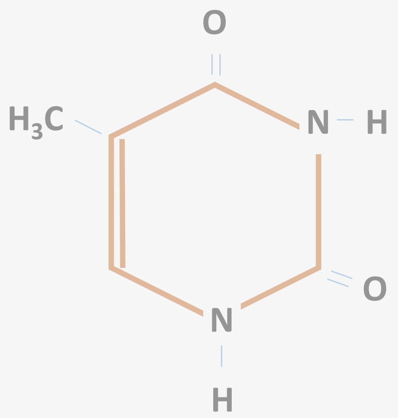
Phosphoric acid

RNA nucleobases

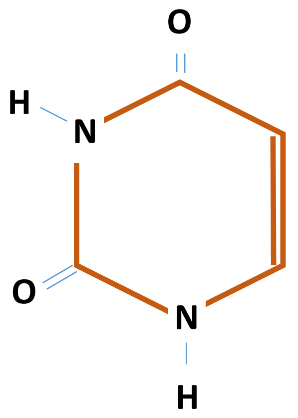
PYRIMIDINES



Cytosine

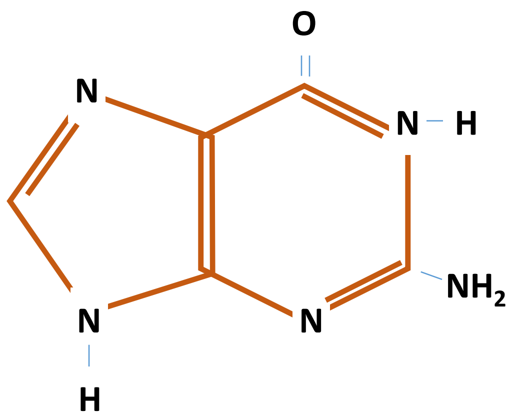


Thymine

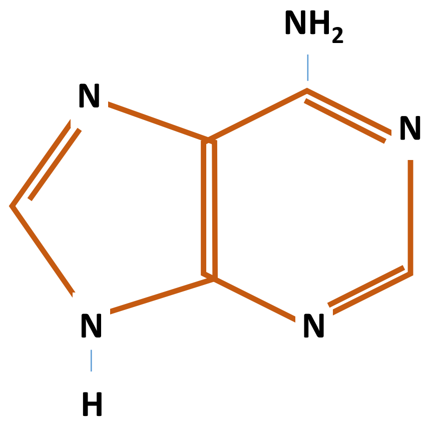


Uracil

PURINES

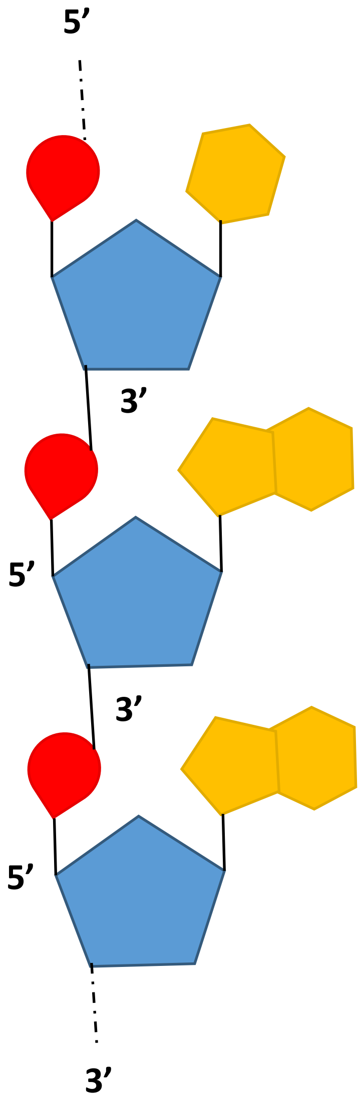


Guanine

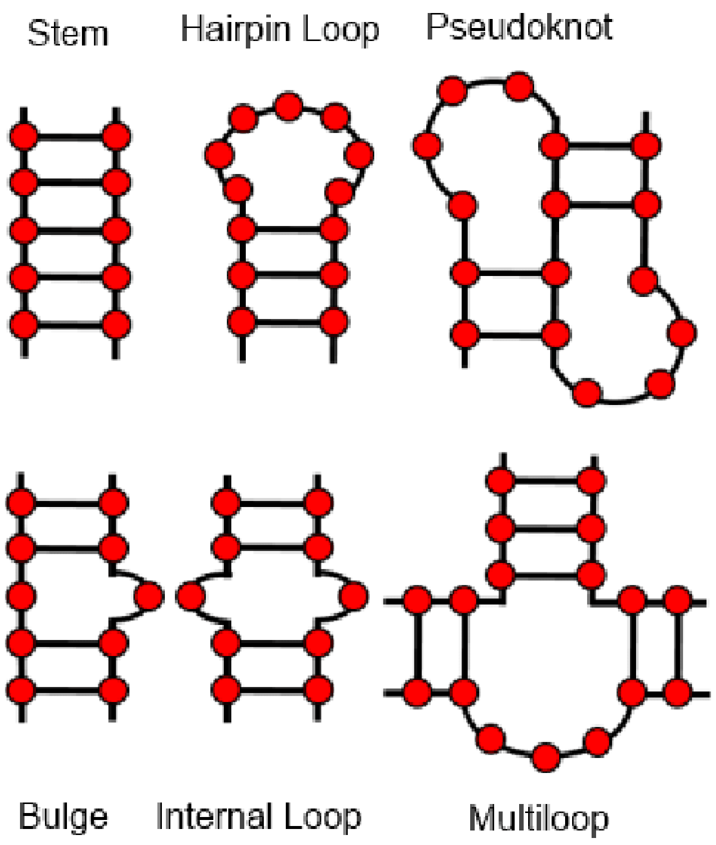


Adenine

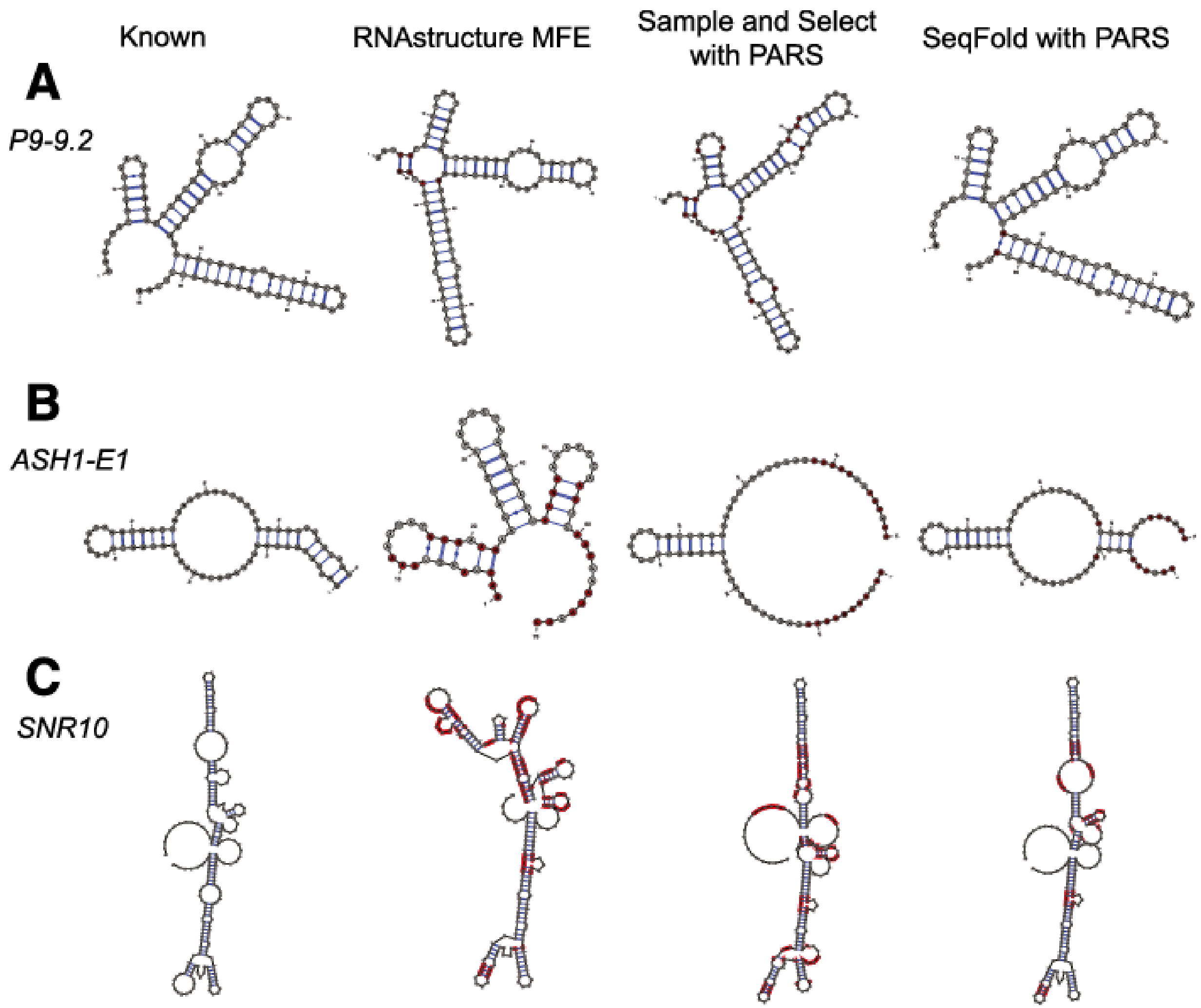
RNA primary structure: chain of nucleotides with phosphodiester bonds.



RNA secondary structure

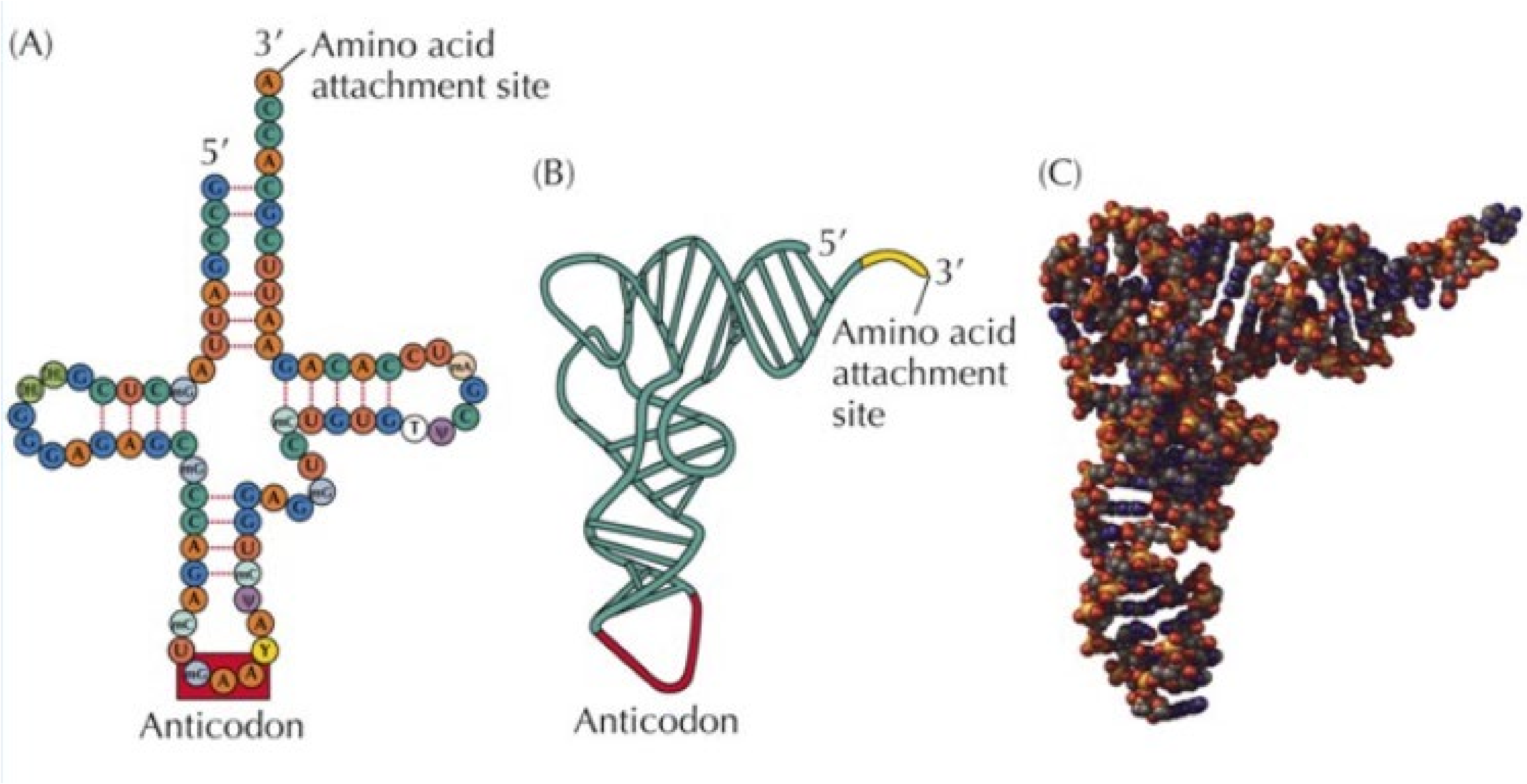


Source: Manish Kumar Gupta, ResearchGate



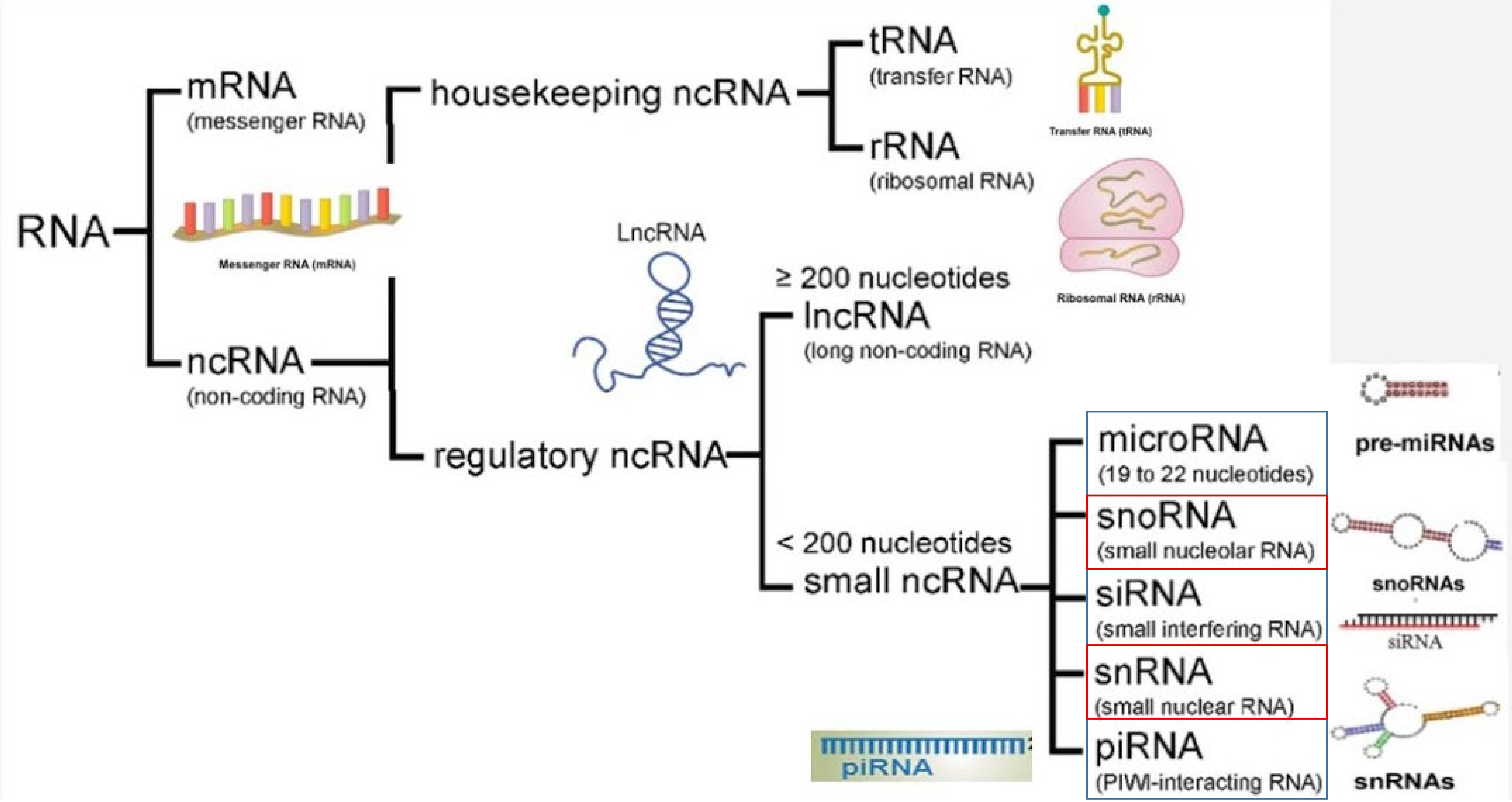
Source: Zhengqing Ouyang, ResearchGate

RNA tertiary structure: tRNA



Source: ASM Press and Sinauer Associates

Main types of RNA



Main differences DNA/RNA

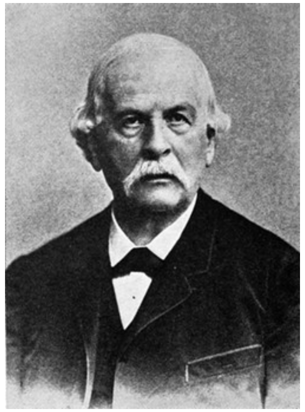
Bases	A, G, C, T	A, G, C, U
Strand	Double stranded	Single stranded
Structure	Antiparallel helix	Hairpin and loops
Sugar	Deoxyribose	Ribose
Location	Nuclear or mitochondrial	Nuclear or cytoplasmic
Lifetime	Long	Short
Process	Transcription	Translation
Types	Nuclear DNA, mtDNA	mRNA, tRNA, rRNA, miRNA, siRNA, ribozyme

Features of hereditary material

- **Stable way to store information.** Instructions for all traits and functions.
- **Auto-replicate with fidelity**.
- **Express the information**. Central Dogma of Biology DNA->RNA->Protein

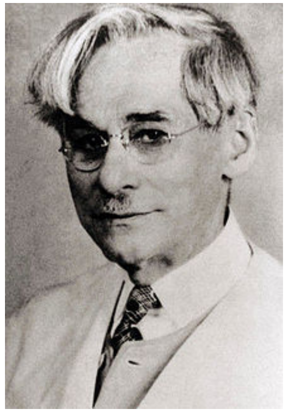
Pioneers in DNA structure and composition

Friedrich Miescher, 1869

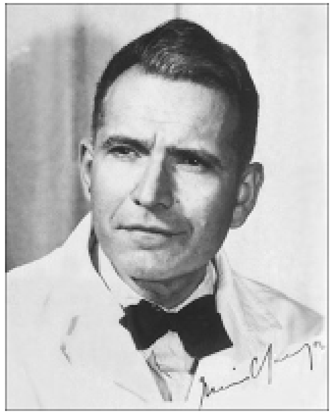


Richard Altmann, 1889

Albrecht Kossel, 1910



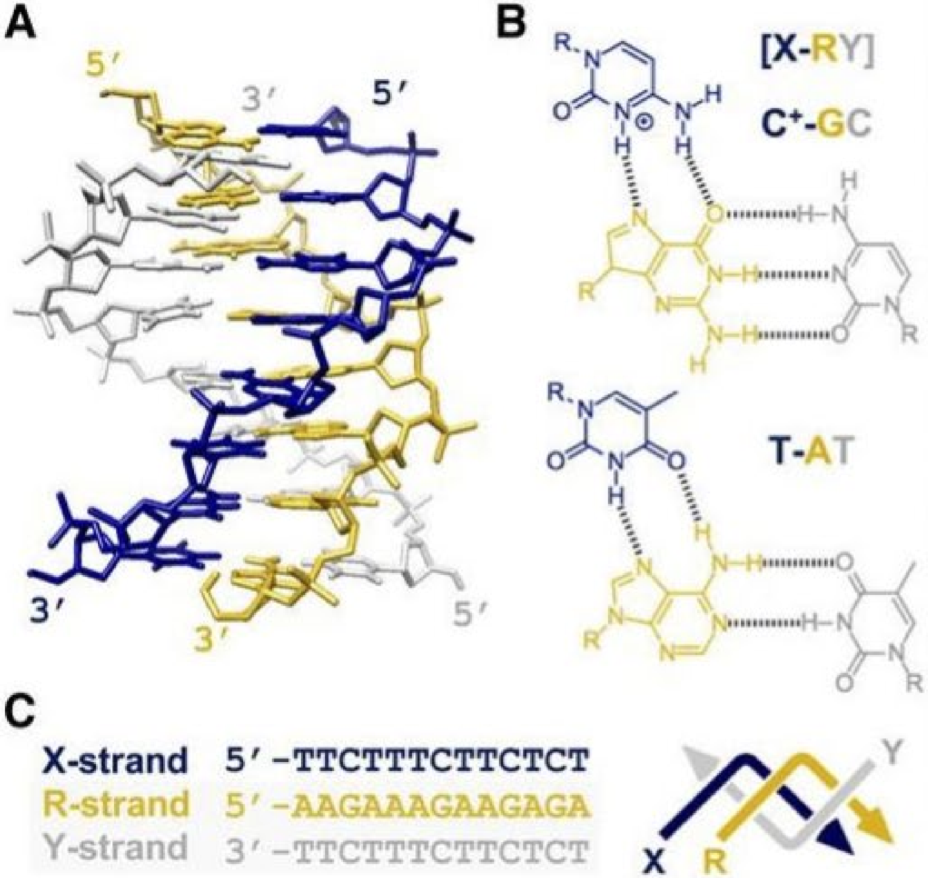
Phoebus Levene, 1920



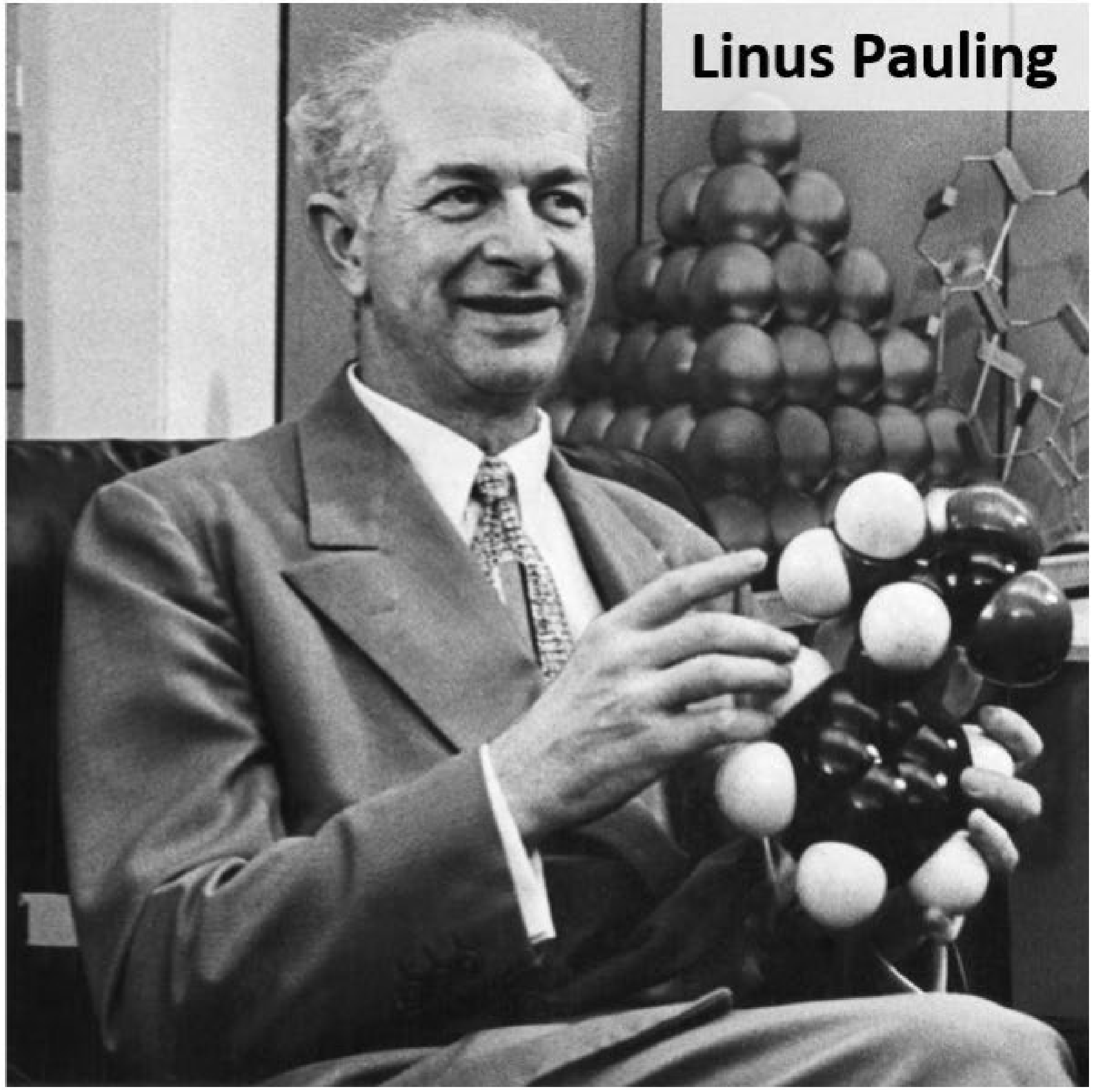
Erwin Chargaff, 1940

Nuclein → **Nucleic Acid** → **Nucleobases** → **Phosphates and Riboses** → **A-T & C-G proportions**

Triple Helix



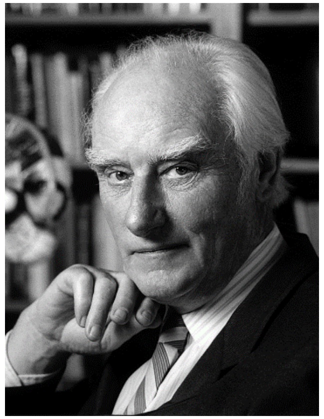
https://doi.org/10.1093/nar/gkx1230



Pioneers in DNA structure and composition

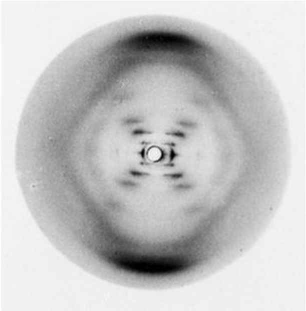
Rosalind Franklin, 1953

Maurice Wilkins, 1953

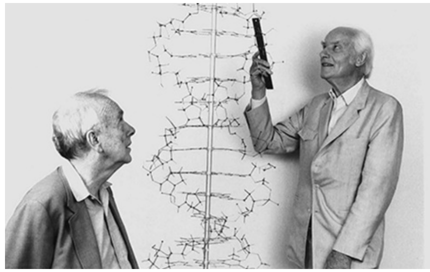


Francis Crick, 1953

James Watson, 1953



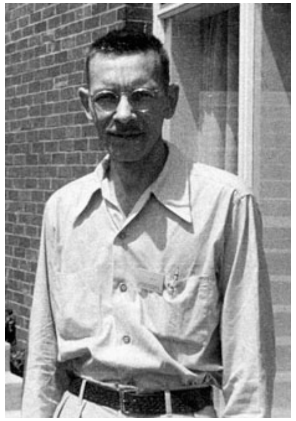
X-ray crystallography ⟷ **Tridimensional structure**



Pioneers in DNA function

Frederick Griffith, 1928

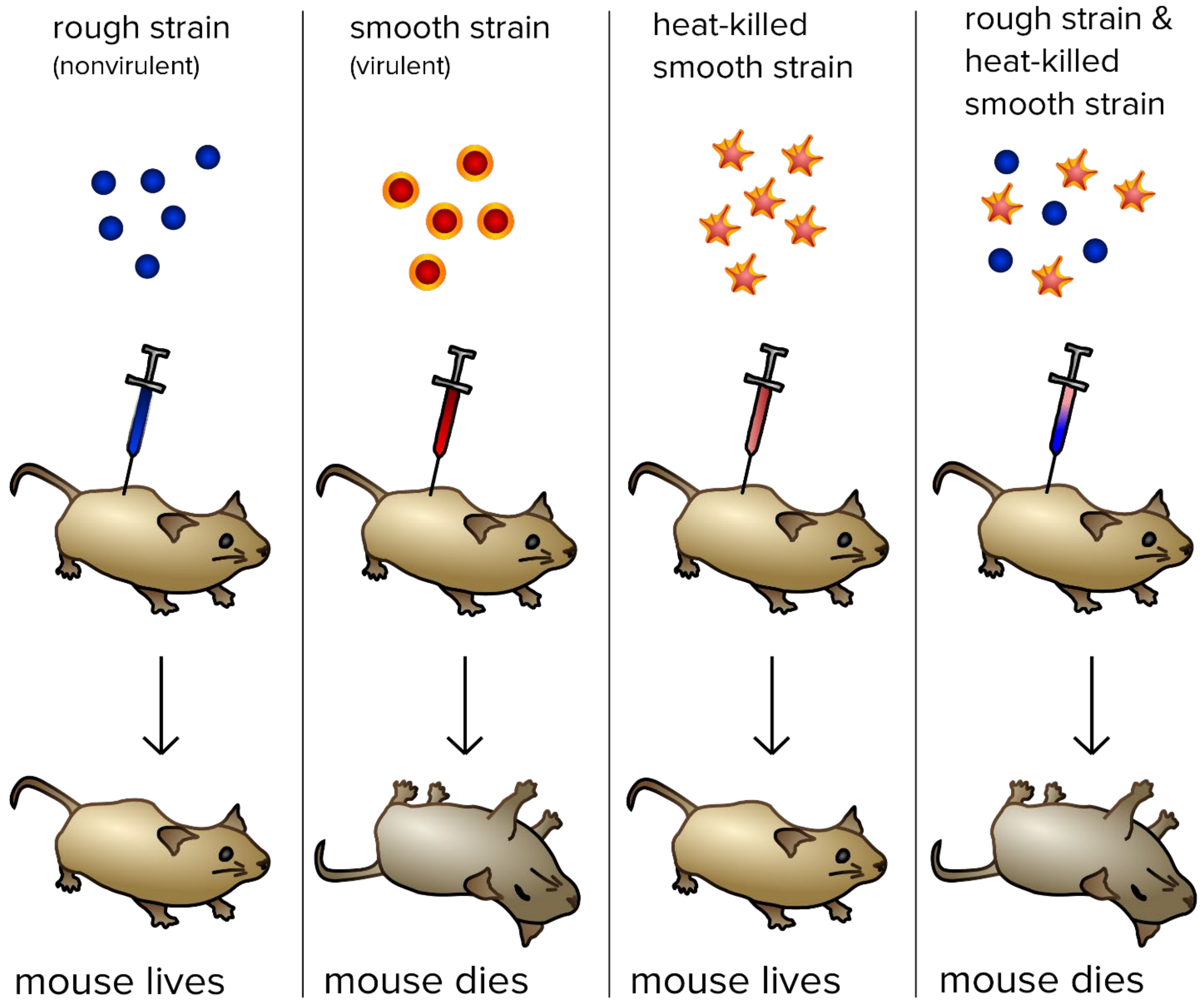
Oswald Avery, 1944



Alfred Hershey, 1952

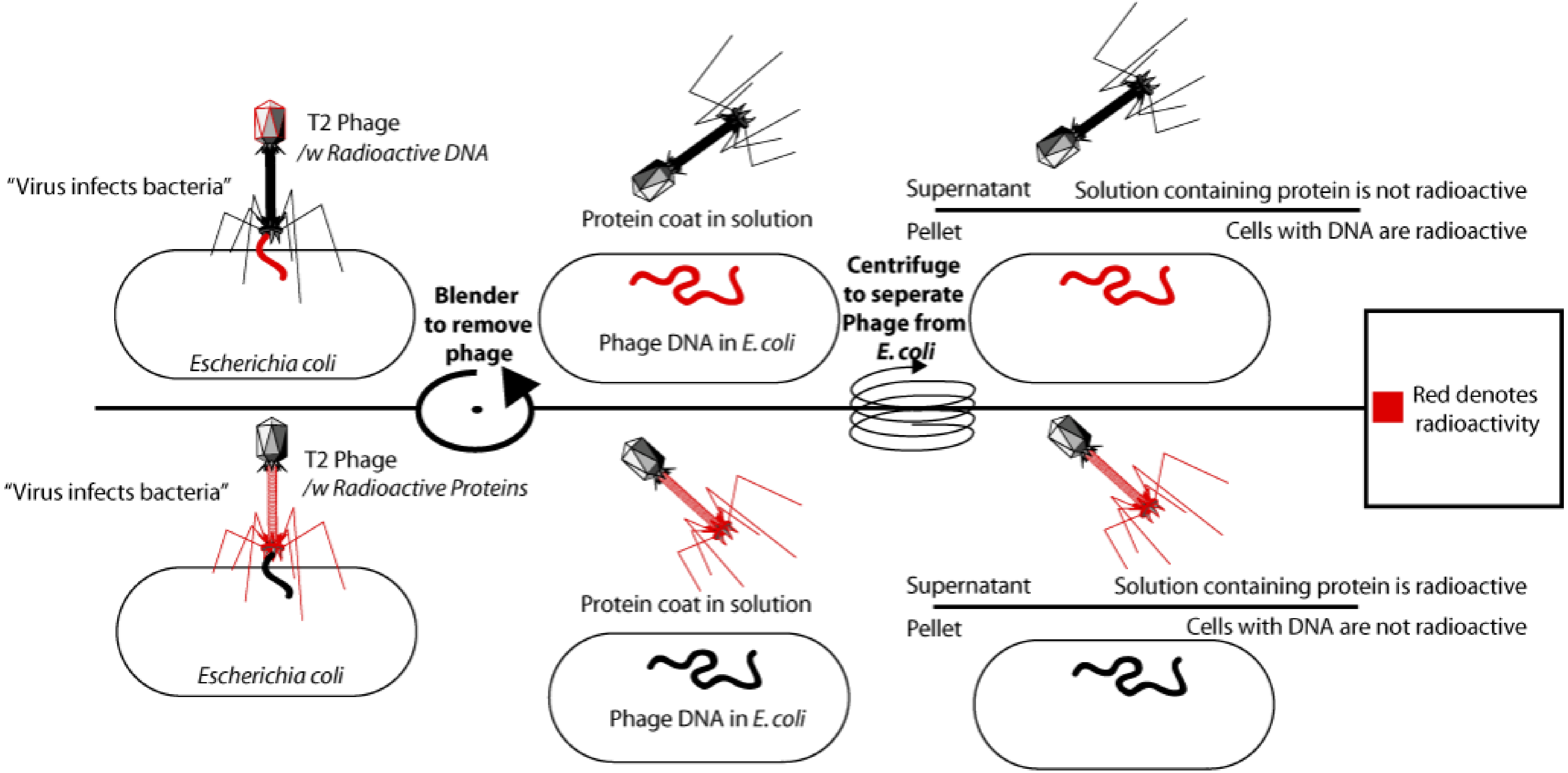
Martha Chase, 1952

Transformation of bacteria → **The Transforming Principle** → **Bacteriophages**



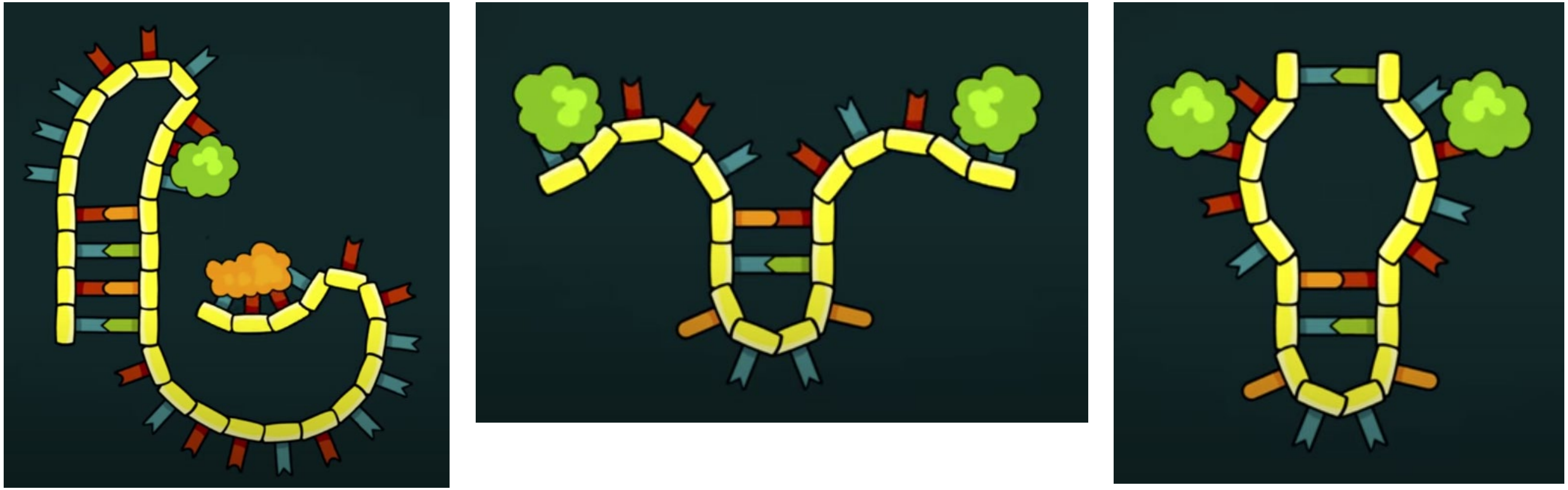
Source: Khan Academy

Hershey & Chase Experiment



Source: Wikipedia

RNA World Hypothesis



- **LUCA** (Last Universal Common Ancestor).

- RNA strands would have served as templates for **auto-replication**.

- Catalitic activity of **ribozimes** (autocatalitic and non-autocatalitic) would allow the acquisition of new "functions".

Source: Stated Clearly

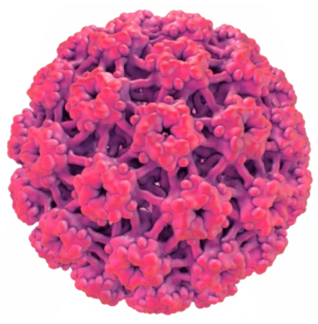
Baltimore Classification of Virus

DNA VIRUS:
GROUP I: double strand
GROUP II: one strand

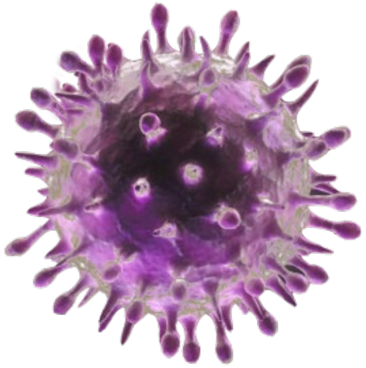
RNA VIRUS:
GROUP III: double strand
GROUP IV: one strand (+)
GROUP V: one strand (-)

DNA VIRUS OR RNA REVERSE TRANSCRIPTASE:
GROUP VI: RNA one strand
GROUP VII: DNA double strand

DNA VIRUS:
GROUP I: double strand

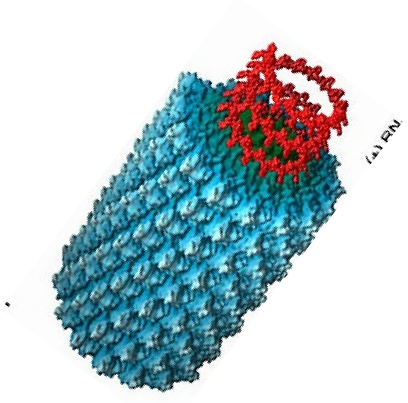


Huma papiloma virus

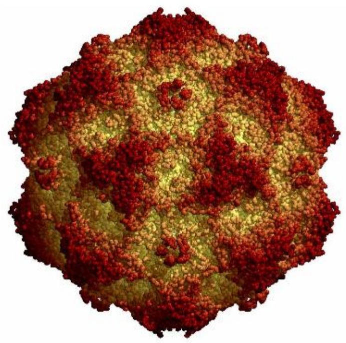


Chickenpox virus
Herpes virus

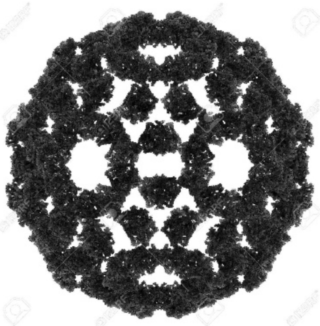
DNA VIRUS:
GROUP II: one strand



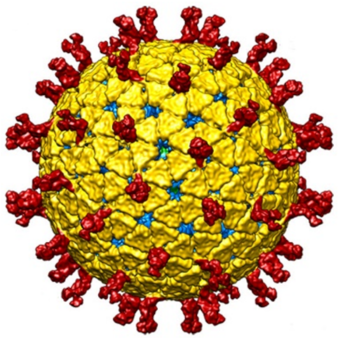
Tobacco mosaic virus



Parvovirus
(fifth disease)

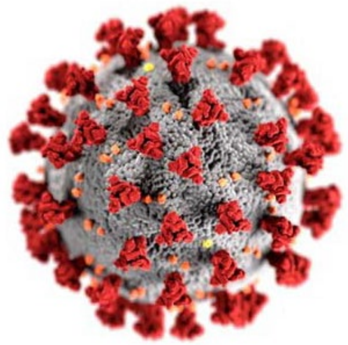


Bluetongue virus

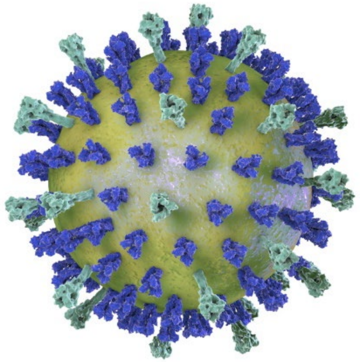


Rotavirus
(gastroenteritis)

RNA VIRUS:
GROUP III: double strand



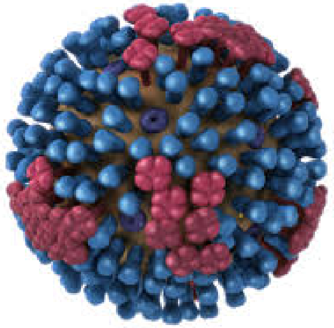
SARS-CoV-2



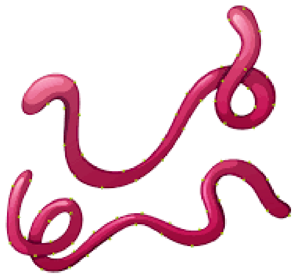
MERS

Yellow fever

RNA VIRUS:
GROUP IV: one strand (+)



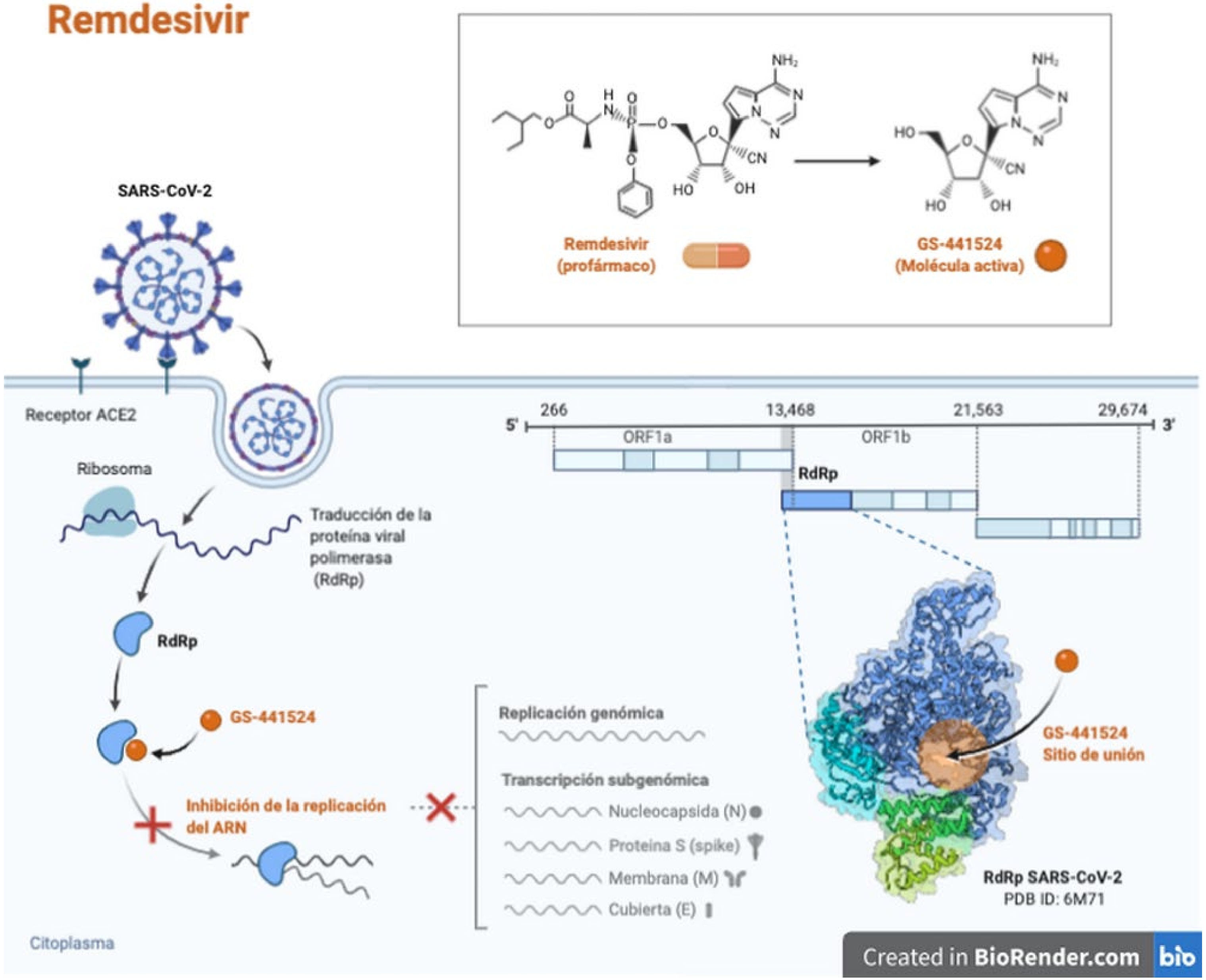
Influenza virus



Ebola virus

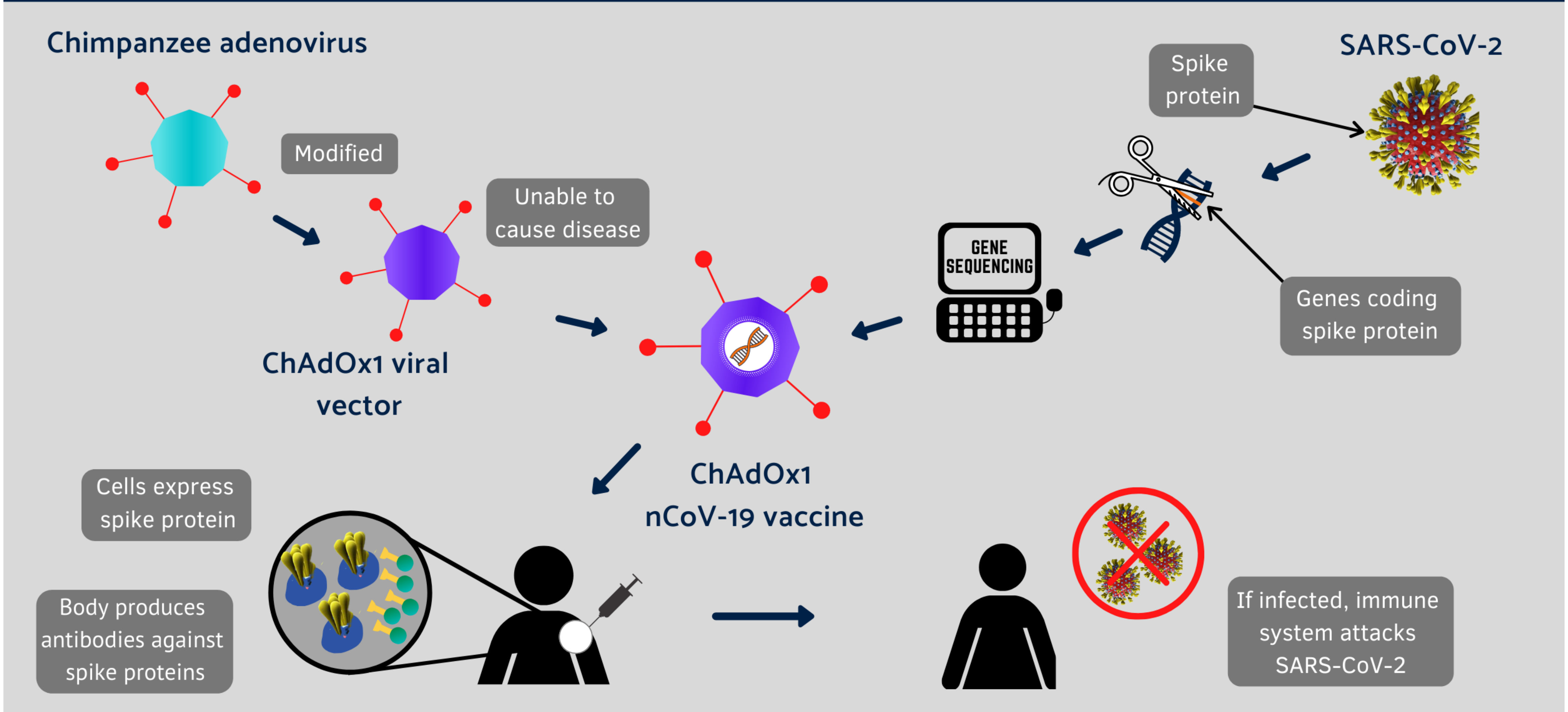
RNA VIRUS:
GROUP V: one strand (-)

Remdesivir

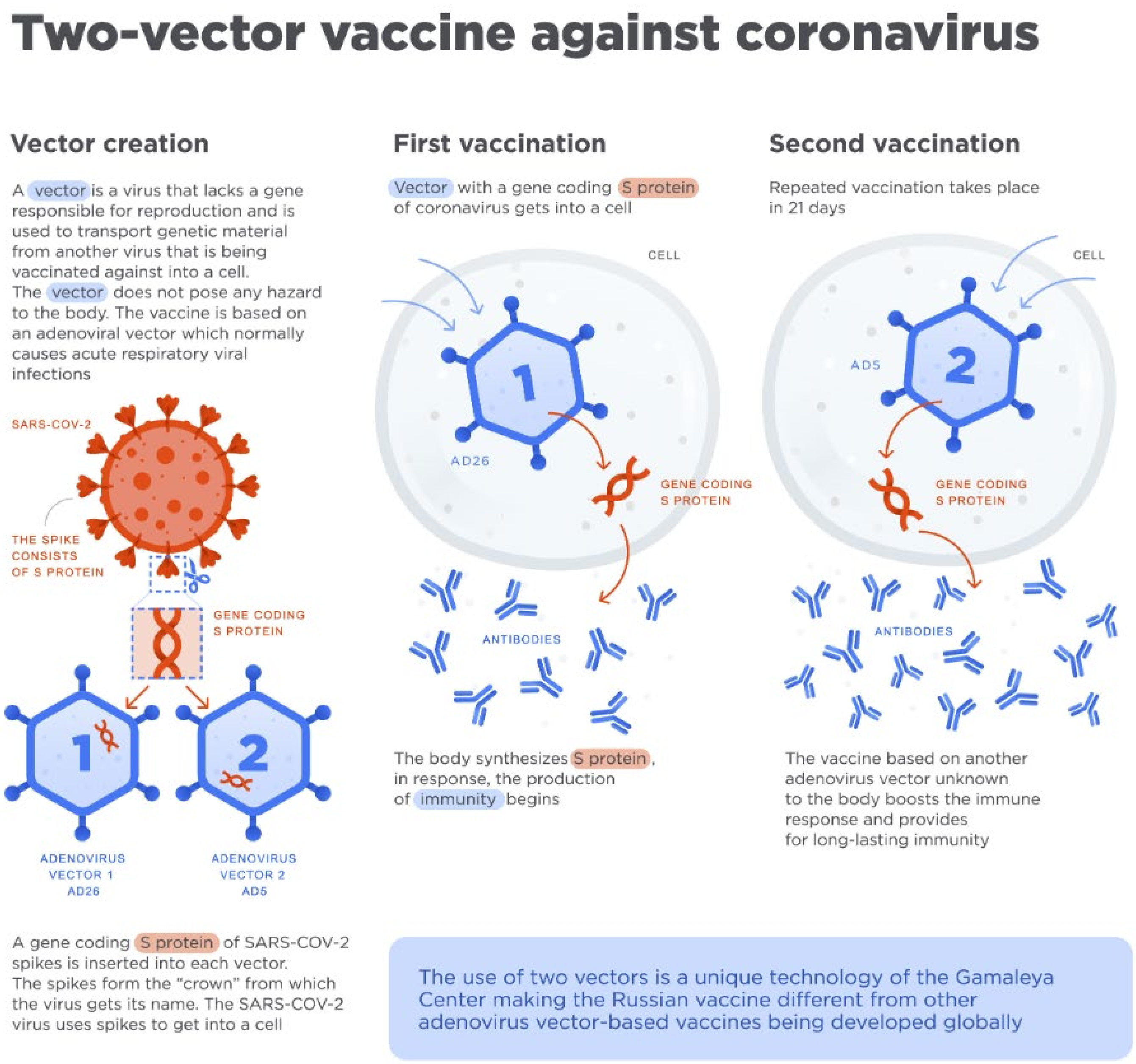


Source: theconversation.com

COVID-19 Oxford Vaccine Trial

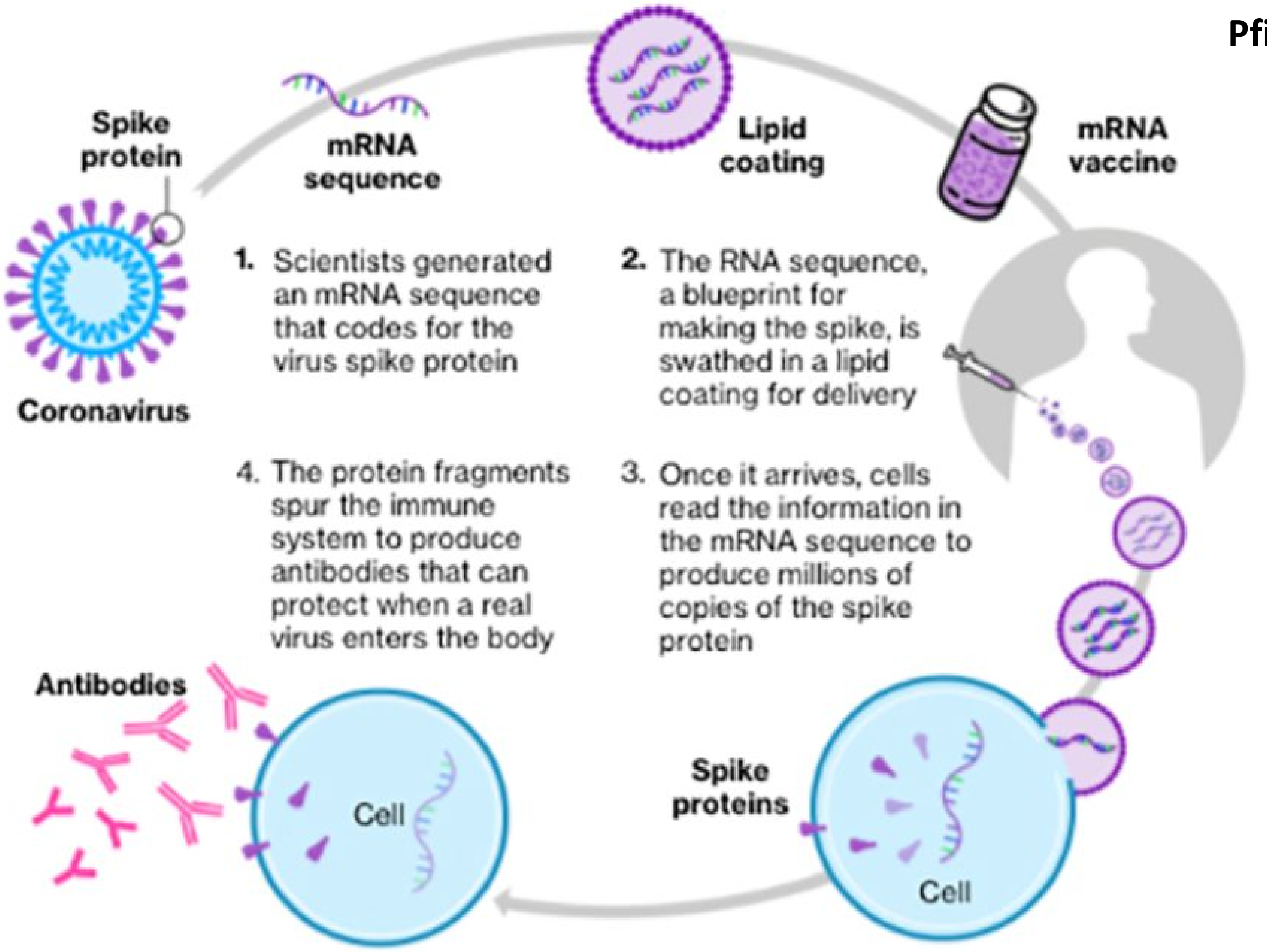


Source: covid19vaccinetrial.co.uk/

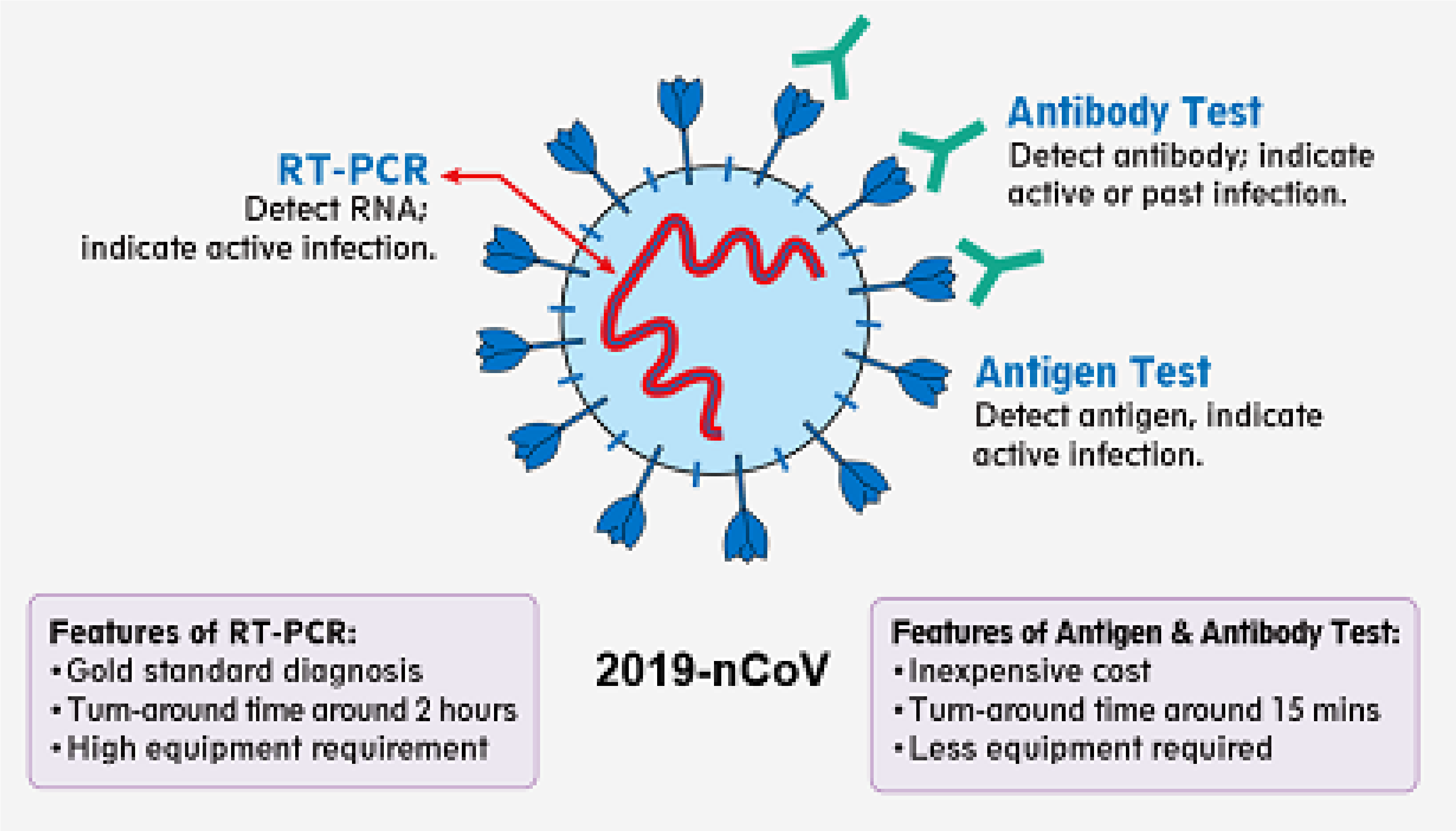


Source: sputnikvaccine.com/

Pfizer, Moderna y Biontech



Fuente: theconversation.com


RT-PCR
Detect RNA;
indicate active infection.
Antibody Test
Detect antibody; indicate
active or past infection.
Antigen Test
Detect antigen, indicate
active infection.
Features of RT-PCR:
•Gold standard diagnosis
•Turn-around time around 2 hours
•High equipment requirement
2019-nCoV
Features of Antigen & Antibody Test:
•Inexpensive cost
•Turn-around time around 15 mins
•Less equipment required

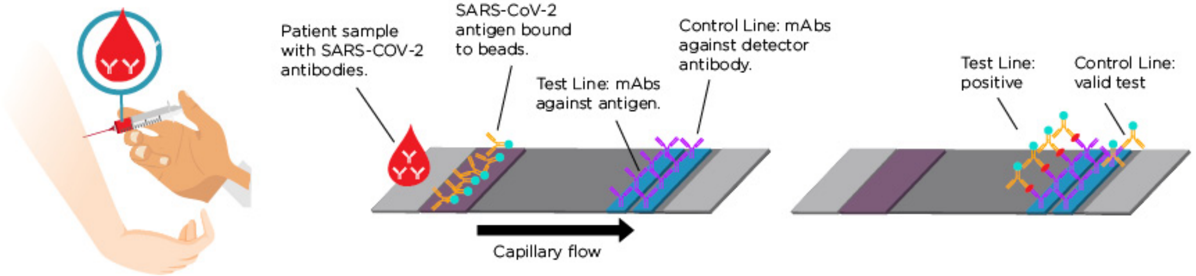
Molecular Tests (Nucleic Acid Detection)

Diagnose active SARS-CoV-2 infections

1. Obtain Specimen: Swab.
2. Extract RNA from specimen and convert to DNA.
3. Amplify by PCR with SARS-CoV-2 specific primers.
4. Interpret results: presence of viral RNA indicates active SARS-CoV-2 infection.

Antibody Tests (Serology)

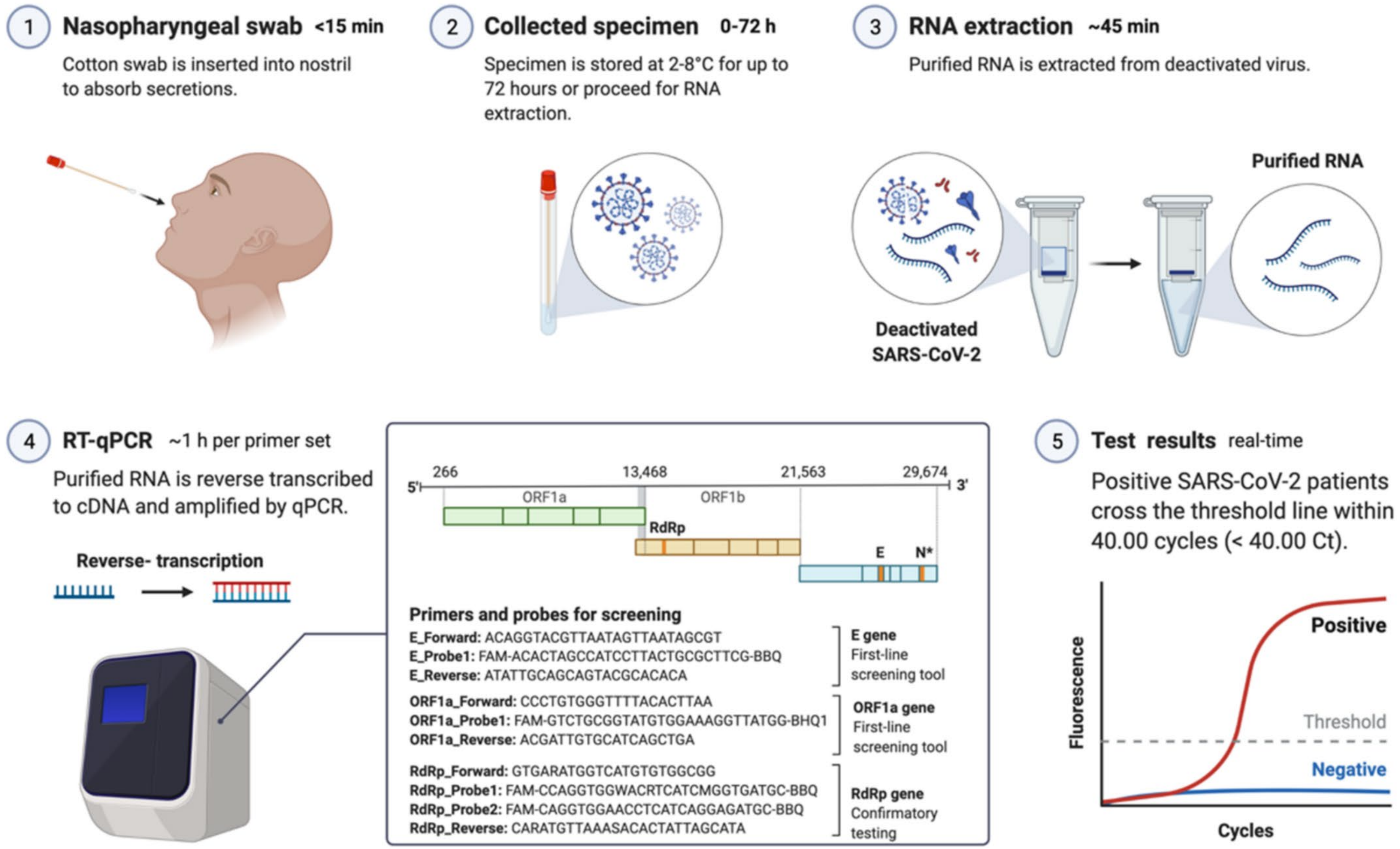
Detect immune response to SARS-CoV-2 exposure



1. Obtain Specimen: Blood Sample.
2. Expose specimen to SARS-CoV-2 specific antigens.
3. Interpret results: color change indicates previous exposure to SARS-CoV-2.

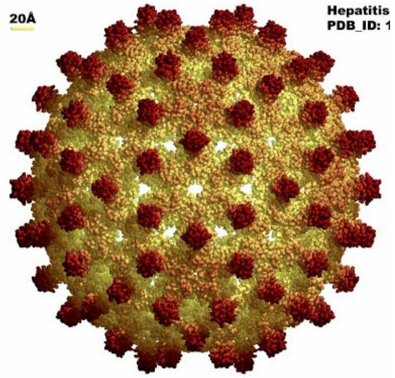
AMERICAN SOCIETY FOR MICROBIOLOGY

COVID-19 Diagnostic Test using RT-qPCR technique

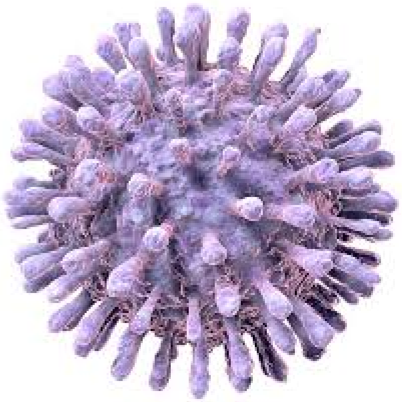


DNA VIRUS OR RNA VIRUS WITH REVERSE TRANSCRIPTASE:

GROUP VI & VII

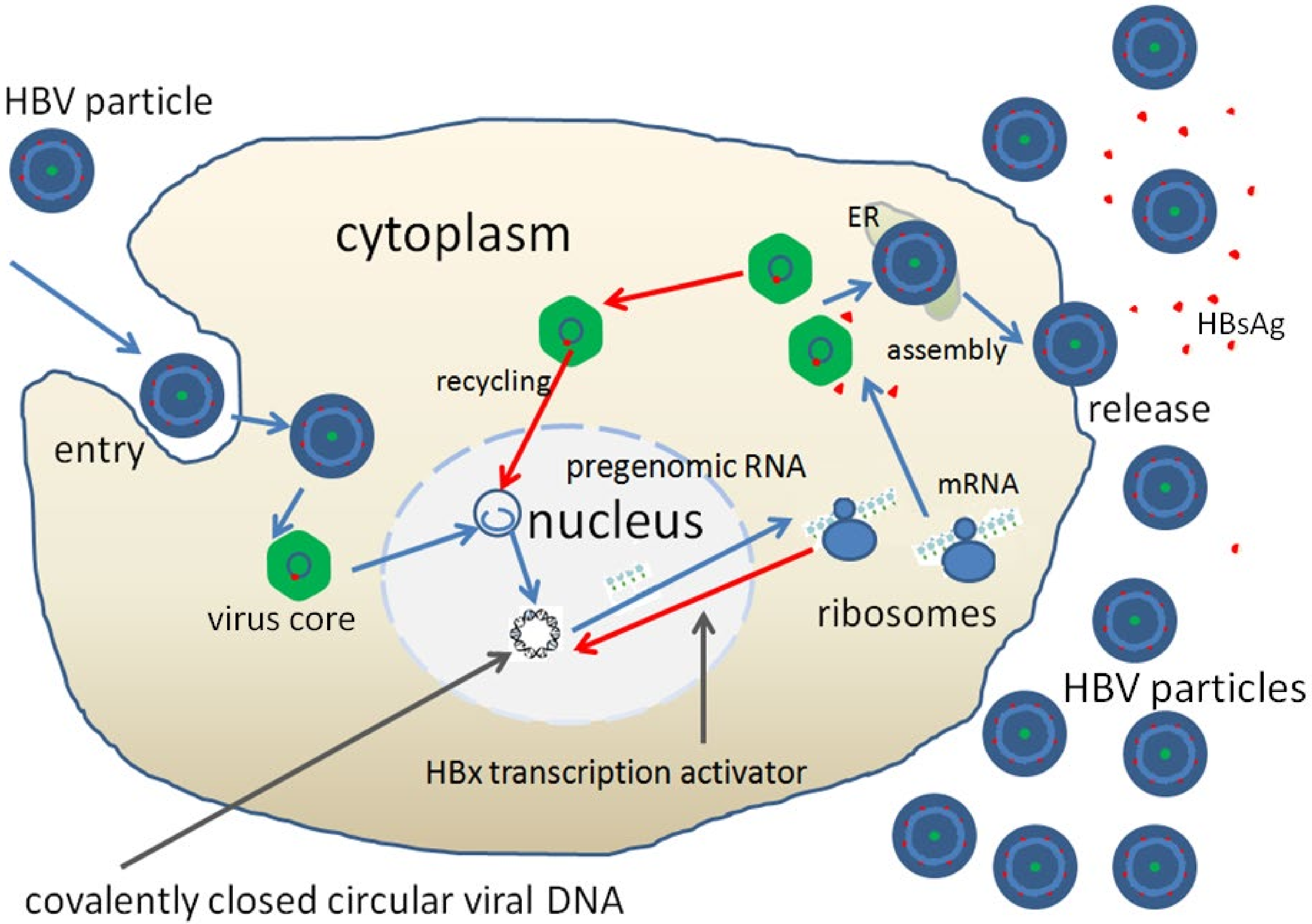


Hepatitis B



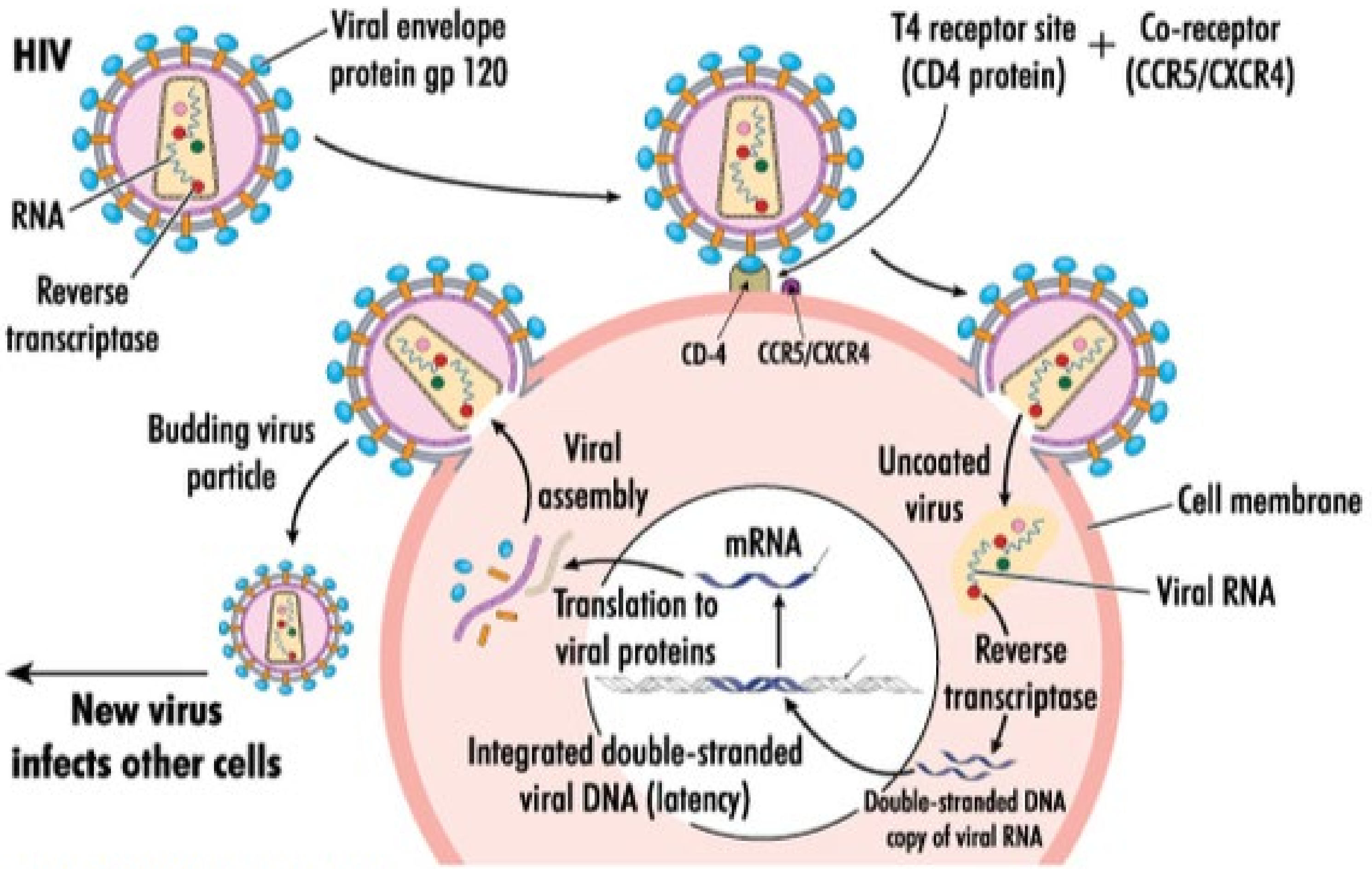
HIV

HBV CYCLE



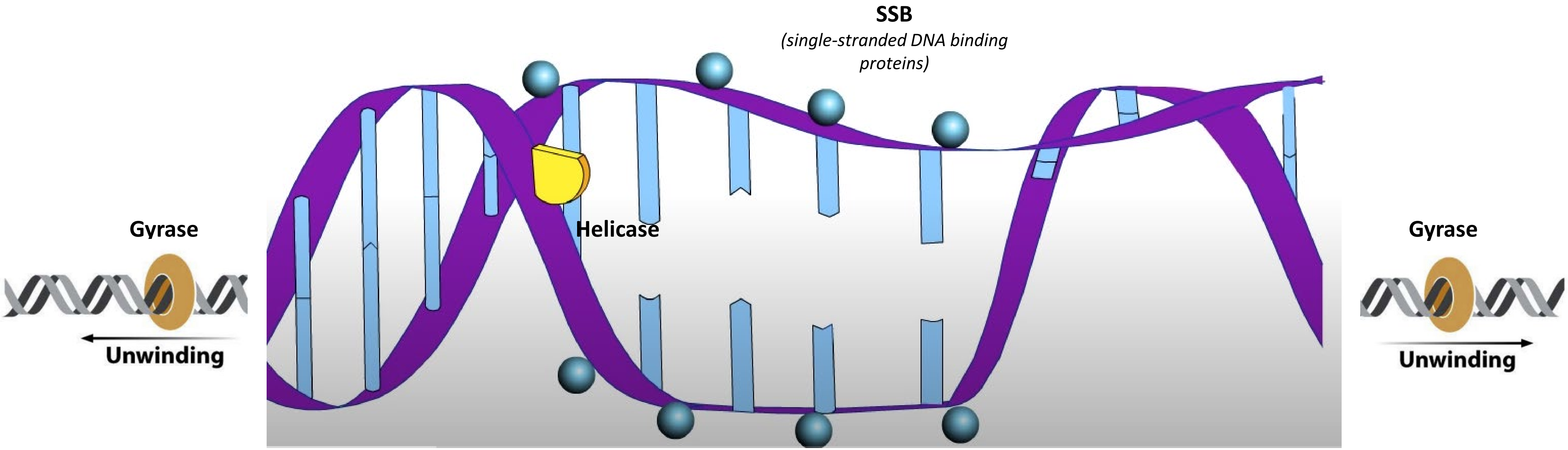
Source: Wikipedia

HIV CYCLE



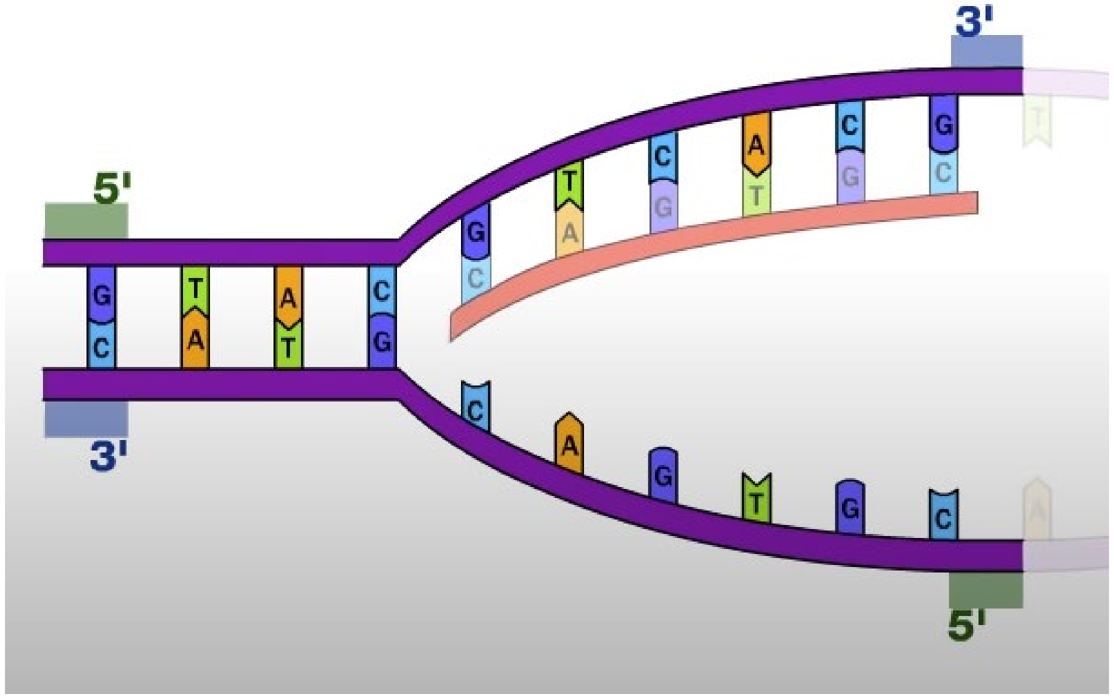
Credit: Blamb/shutterstock.com

DNA Replication



Soruce: https://www.youtube.com/watch?v=YqjbmrQcyfM & Panamericana

DNA Replication

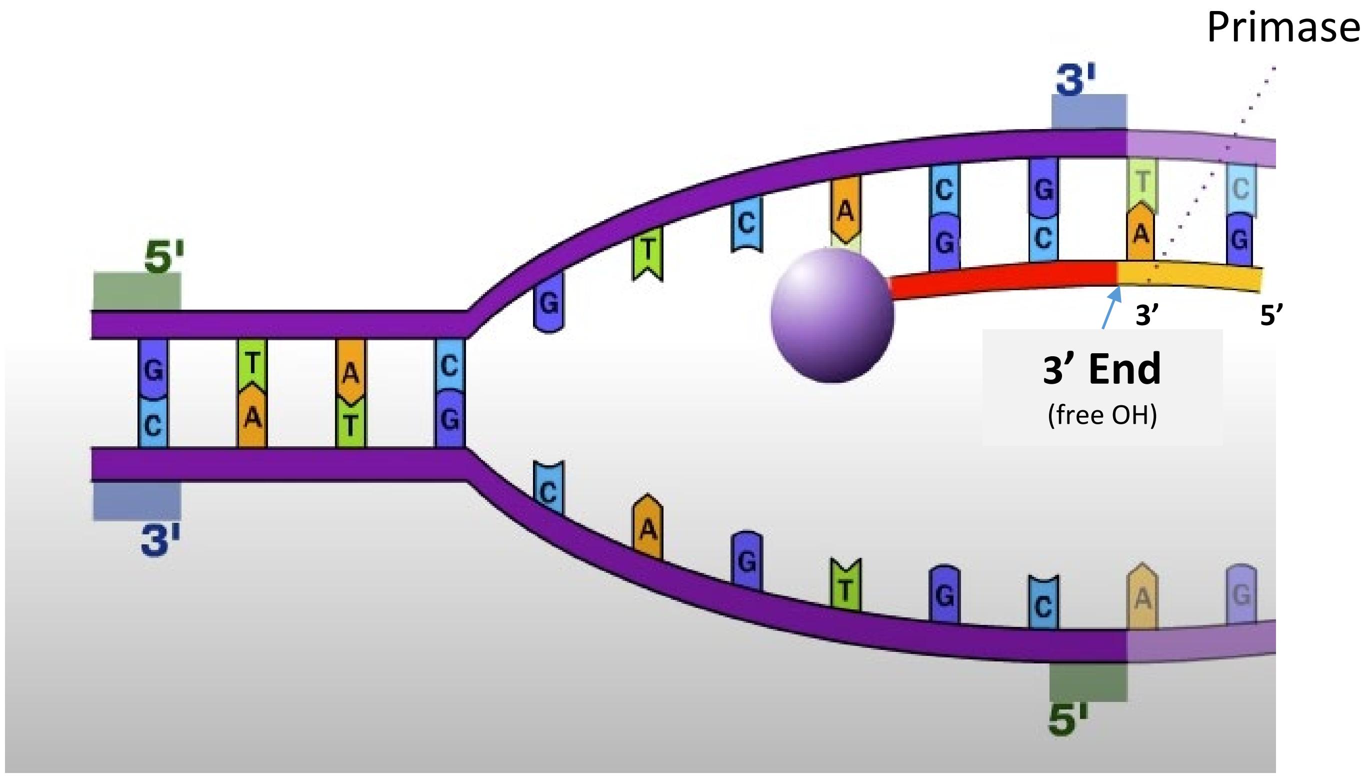


<u>DNA POLYMERASE:</u>

- Needs a double-stranded fragment (*primer*) with a free 3' end.
- Add nucleotides in **5'-3'** direction.

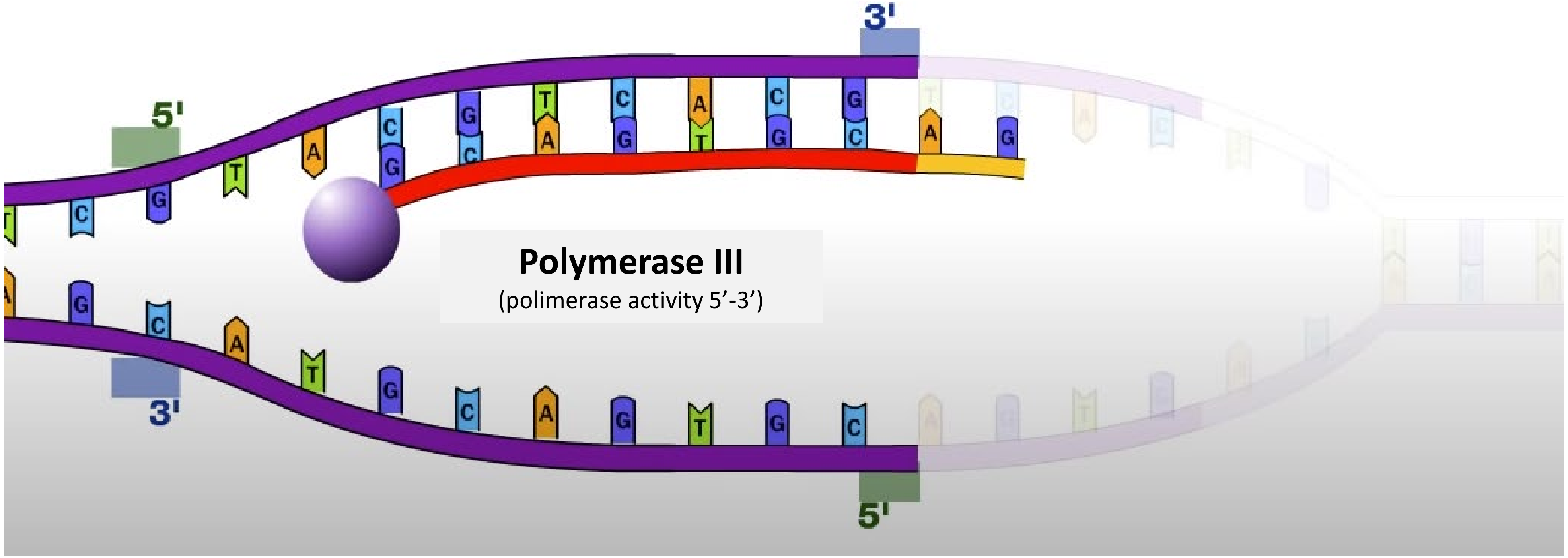
Source: https://www.youtube.com/watch?v=YqjbmrQcyfM

DNA Replication



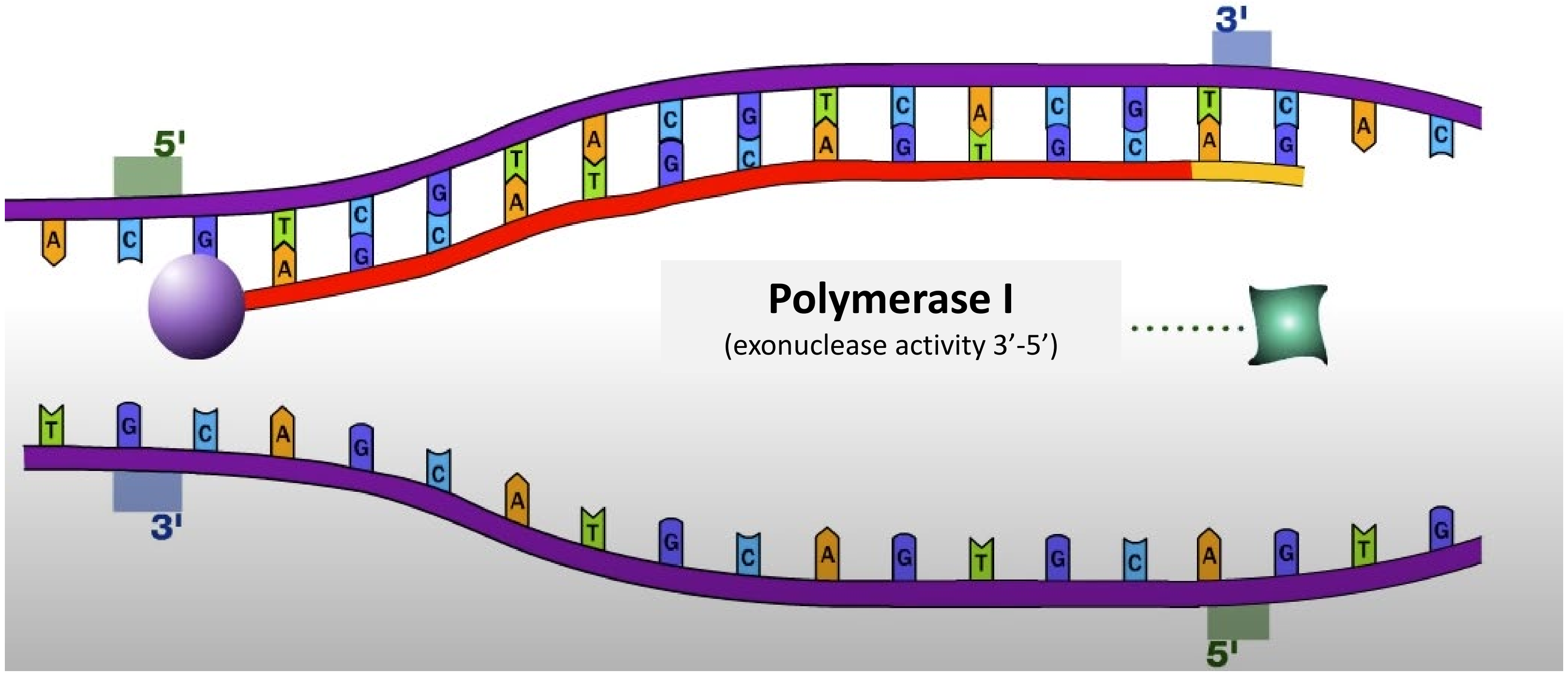
Source: https://www.youtube.com/watch?v=YqjbmrQcyfM

DNA Replication



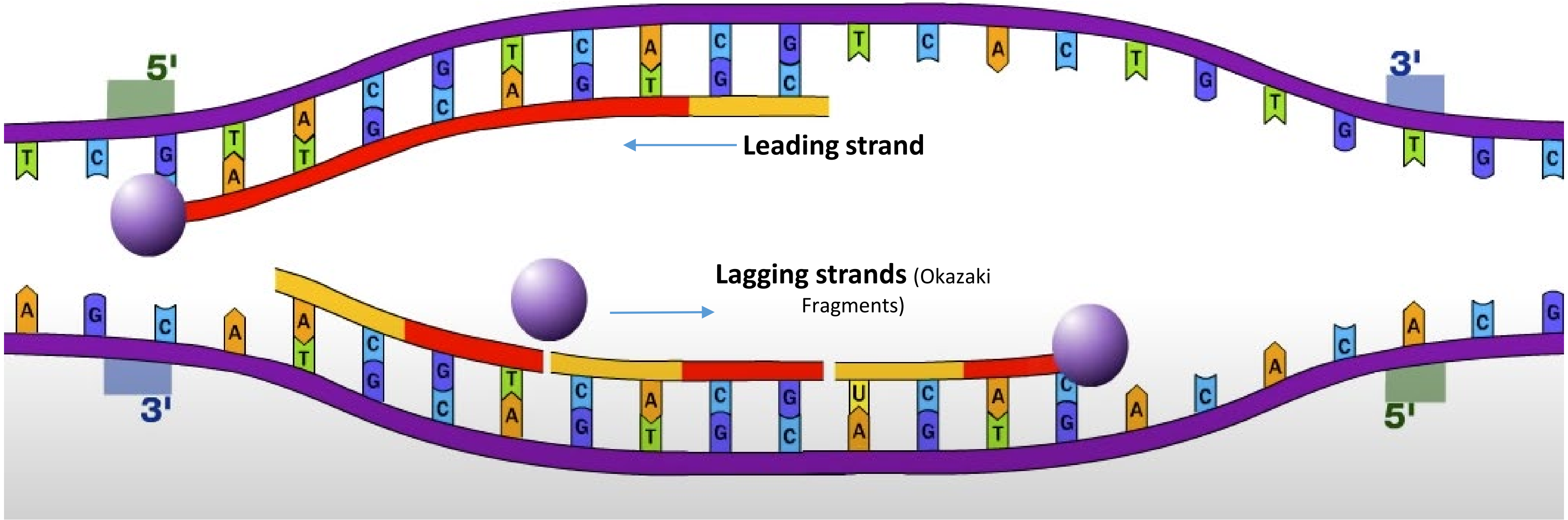
Fuente: https://www.youtube.com/watch?v=YqjbmrQcyfM

DNA Replication



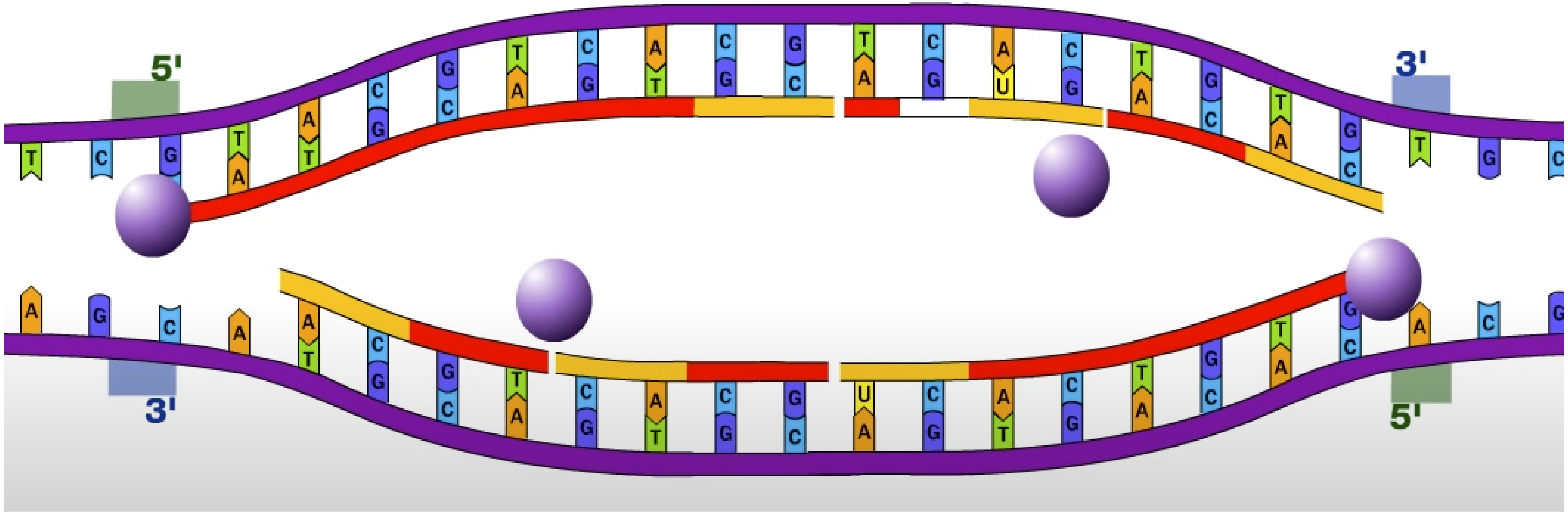
Fuente: https://www.youtube.com/watch?v=YqjbmrQcyfM

DNA Replication



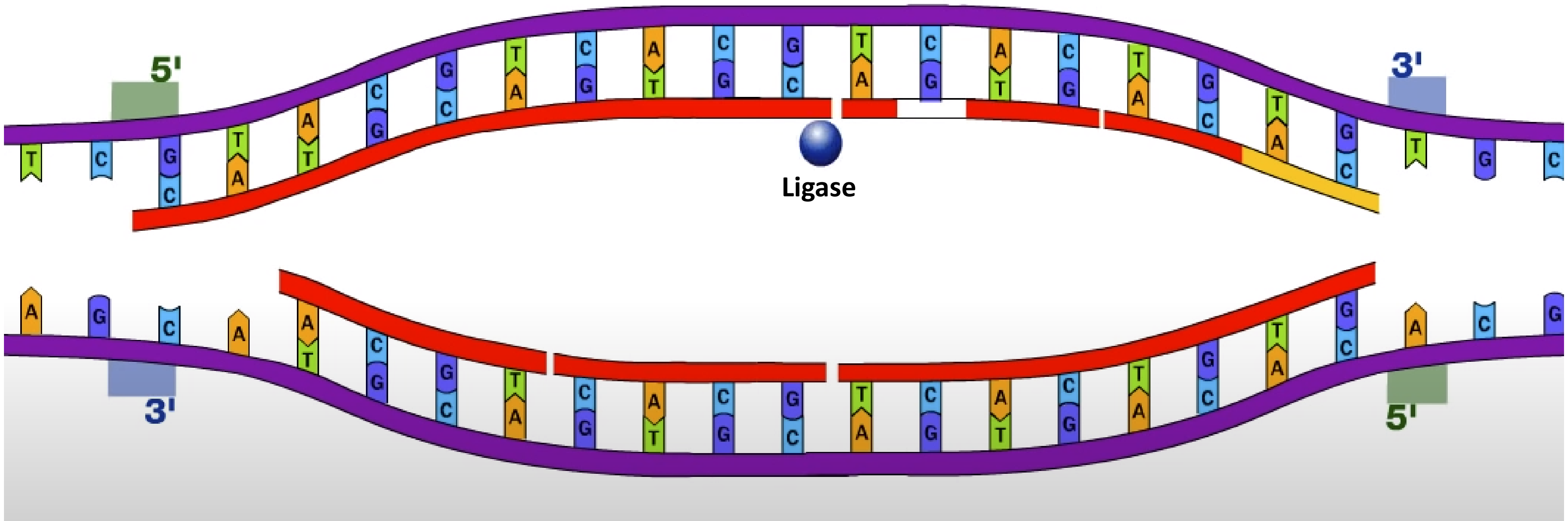
Fuente: https://www.youtube.com/watch?v=YqjbmrQcyfM

DNA Replication



Fuente: https://www.youtube.com/watch?v=YqjbmrQcyfM

DNA Replication

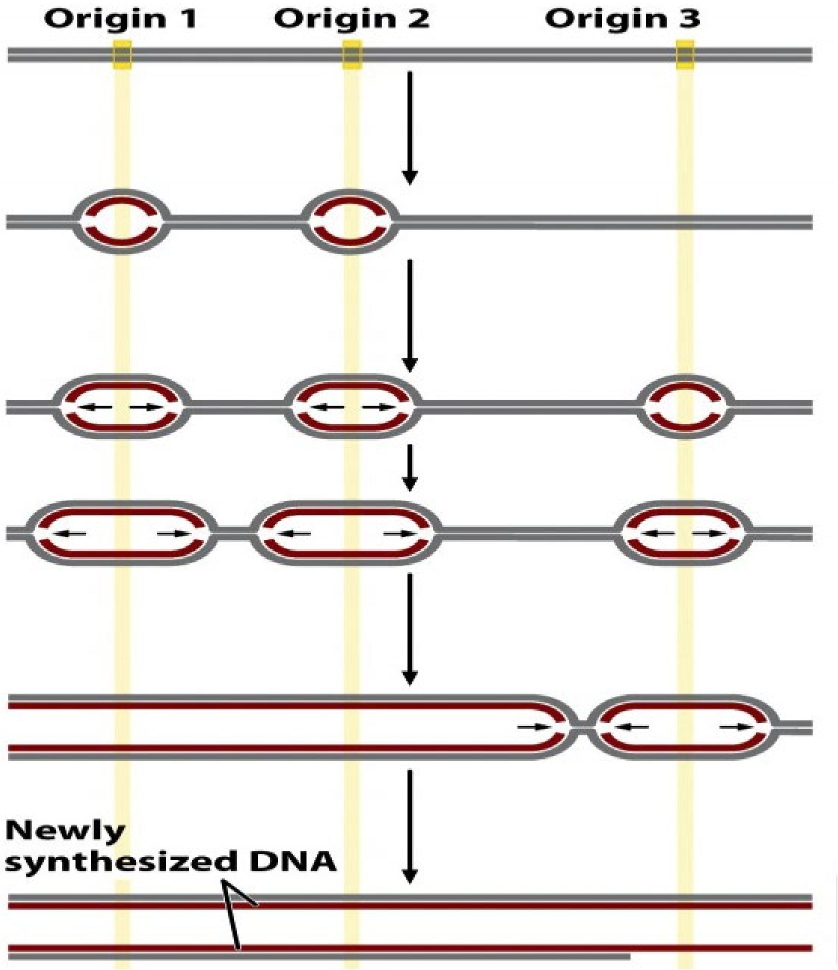


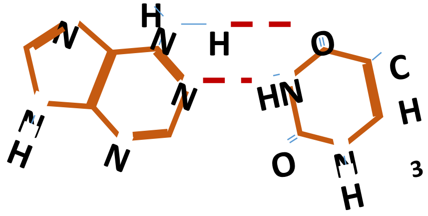
Fuente: https://www.youtube.com/watch?v=YqjbmrQcyfM

DNA Replication

Replication bubbles

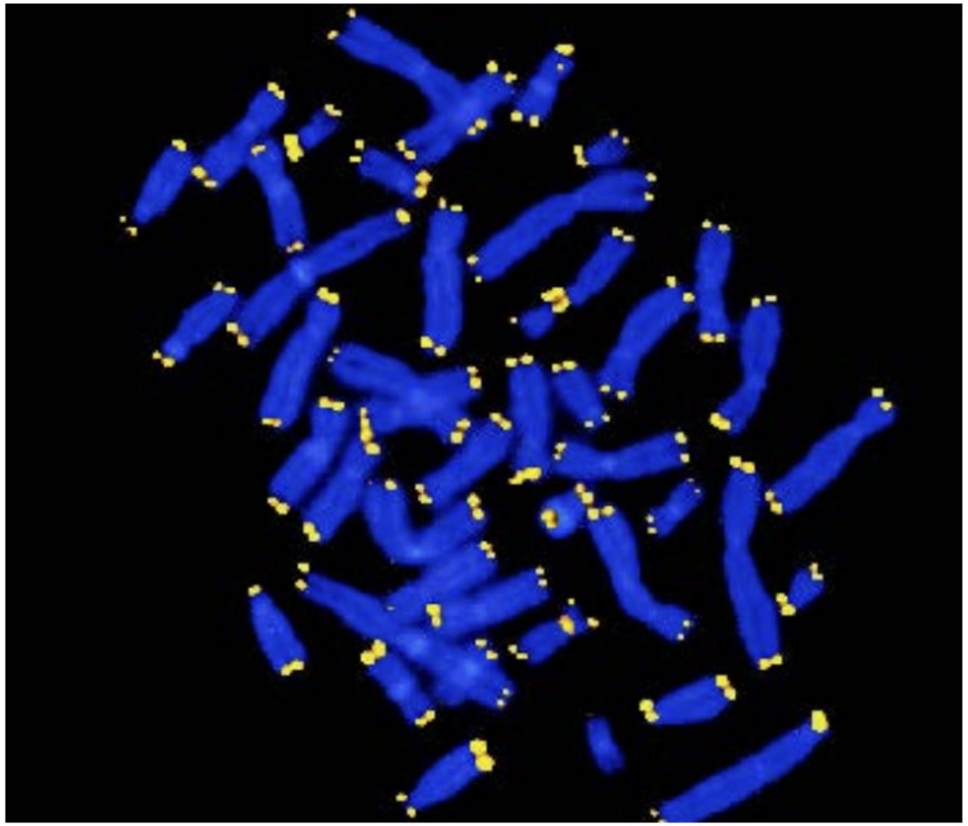
Replication forks





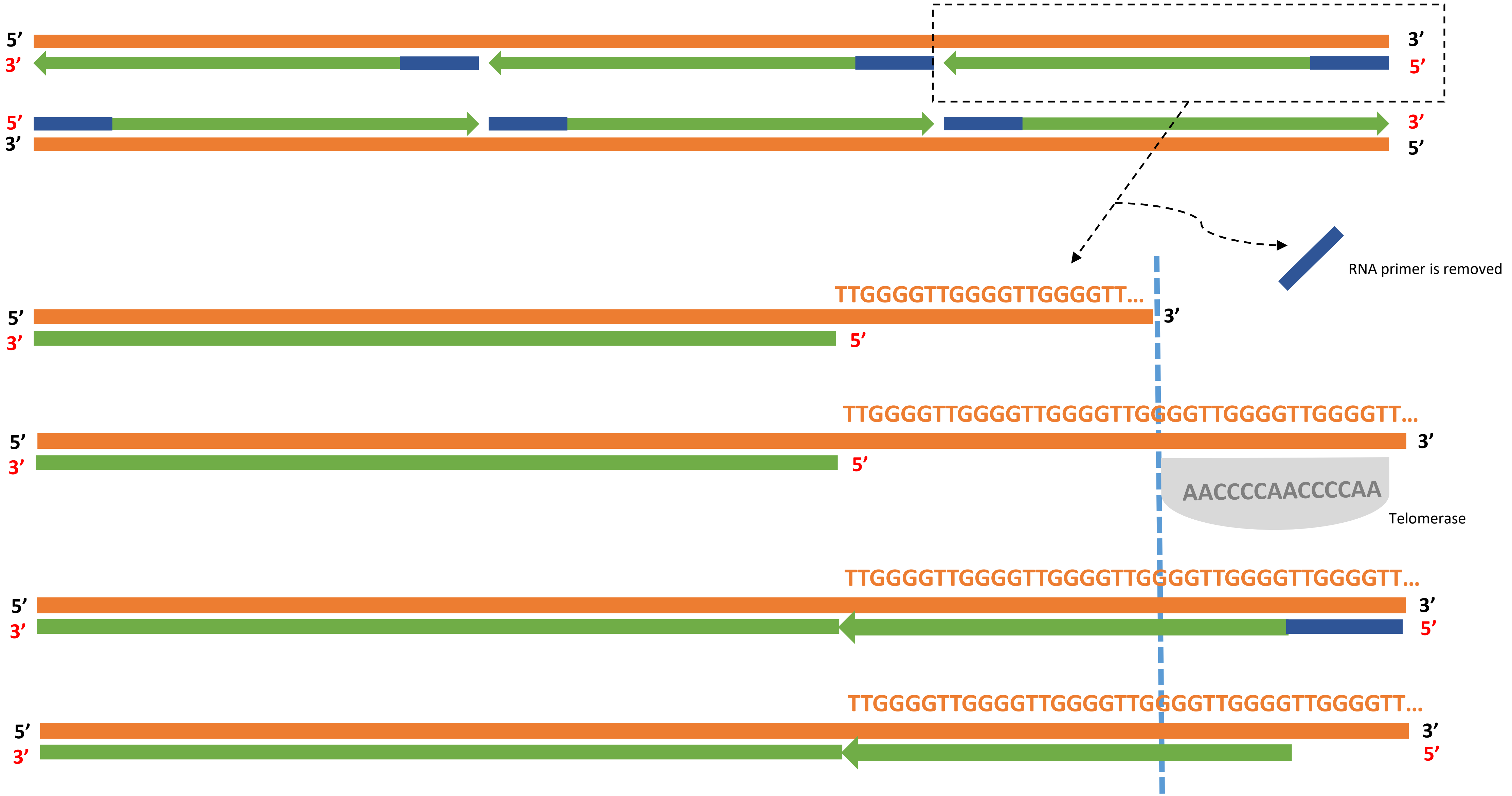
Source: Panamericana

Replication of Telomeres

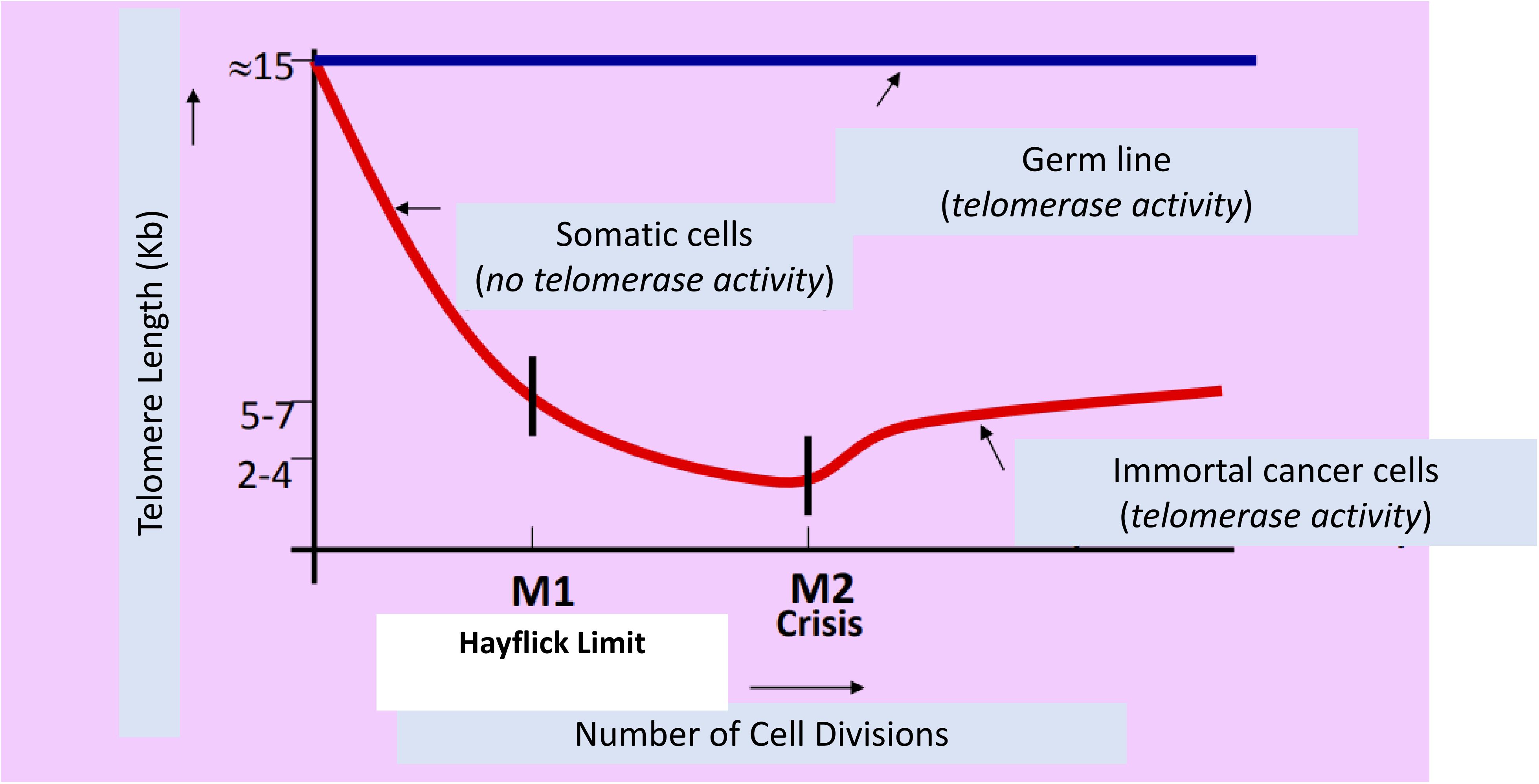


Species	Motif[a] (5′→3′)
Homo sapiens	GGGTTA
Saccharomyces cerevisiae	$G_{1-3}T$
Trypanosoma brucei	GGGTTA
Oxytricha fallax/nova	GGGGTTTT
Tetrahymena thermophila	GGGGTT
Stylonychia lemnae/pustulata	GGGGTTTT

REPLICATION OF TELOMERES



www.rafaelnavajas.eu

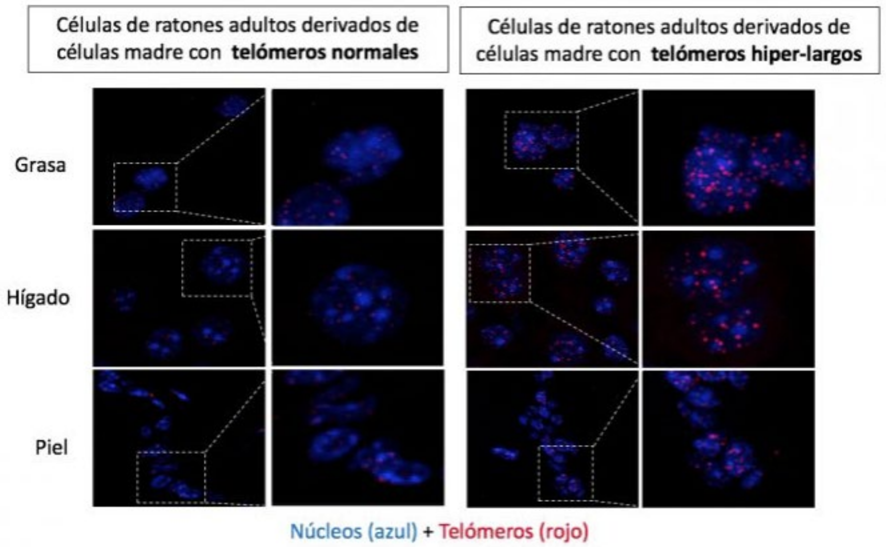


Telomere Length (Kb)
≈15
5-7
2-4
Germ line
(*telomerase activity*)
Somatic cells
(*no telomerase activity*)
Immortal cancer cells
(*telomerase activity*)
M1
Hayflick Limit
M2
Crisis
Number of Cell Divisions

***Nature Communications.* Investigadores del CNIO consiguen los primeros ratones nacidos con telómeros hiperlargos y demuestran que es posible prolongar la vida sin ninguna modificación genética**

17.10.2019

AYUDA A LA INVESTIGACIÓN



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URGENTE

ANIMALES MÁS SALUDABLES EN SU VEJEZ

Científicos españoles crean ratones un 40% más longevos y resistentes al cáncer

- **Los animales viven más y también en mejores condiciones**

Actualizado jueves 13/11/2008 18:00 (CET)

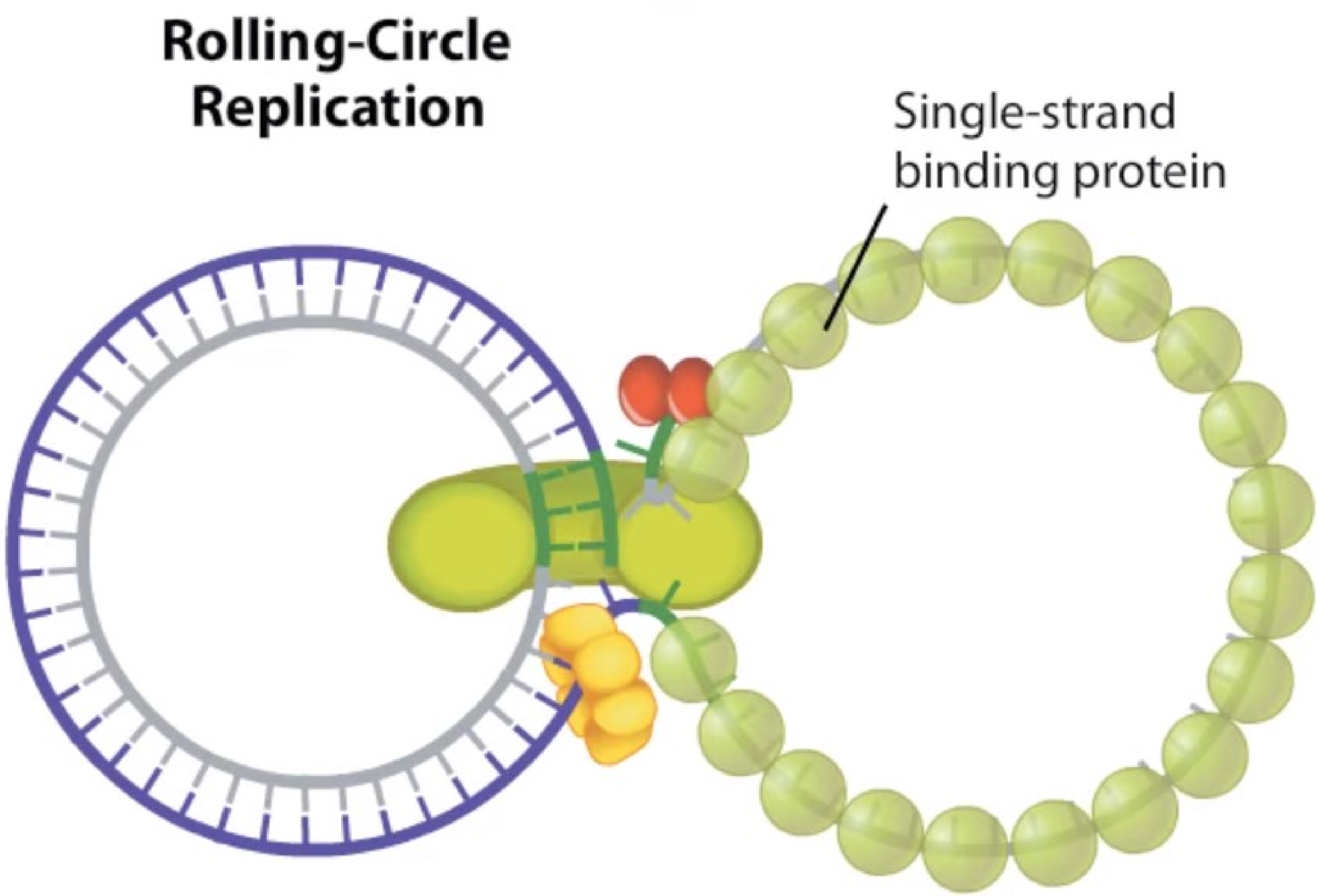
MARÍA VALERIO

MADRID.- Super Ratón, el personaje de dibujos animados de la factoría Terrytoons que volaba por las pantallas de televisión en la década de los ochenta con su capa roja, obtenía los poderes de una alimentación especial. En el laboratorio de María Blasco, en el Centro Nacional de Investigaciones Oncológicas (CNIO), los roedores obtienen sus 'superpoderes' de la telomerasa, una sustancia que protege a las células del envejecimiento y permite a los animales ser un 40% más longevos de lo normal.

Para lograr la ecuación perfecta, el equipo de Blasco probó a modificar genéticamente a los ratones en una doble dirección: aumentando los niveles de telomerasa para que no envejeciesen e incrementando al mismo tiempo la presencia de varios genes supresores tumorales (p53, p16 y p19ARF) para protegerles del cáncer. Para ello, emplearon un modelo de ratón creado también en las mismas instalaciones del CNIO por el equipo de Manuel Serrano y que es 'inmune' al cáncer gracias a sus modificaciones genéticas; y sobre ese ejemplar aumentaron la proteína TERT, responsable de la regeneración de los telómeros.

Source: CNIO, El Mundo

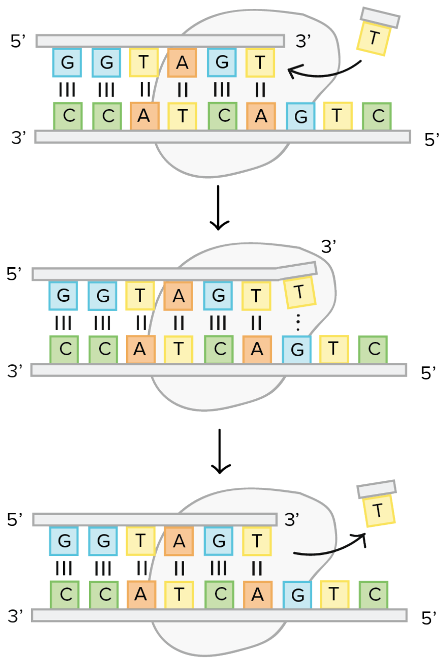
DNA Replication in bacteria



Source: https://youtu.be/ZDqsojQ8A5k

Proofreading

Proof-reading

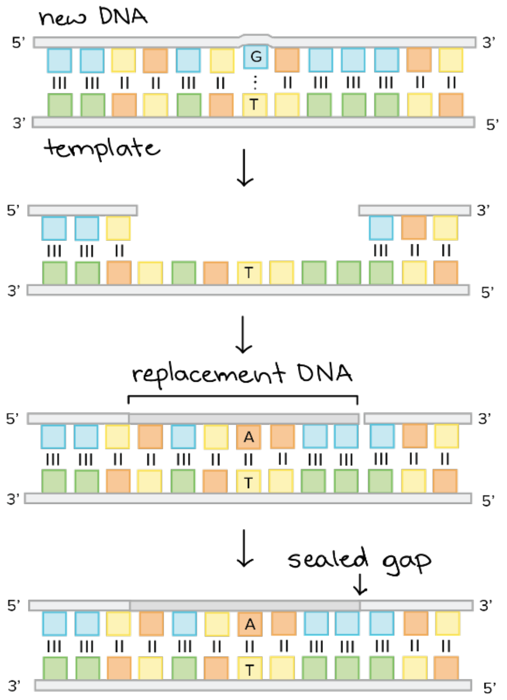


Polymerase adds an incorrect nucleotide to the new strand of DNA.

Polymerase detects that bases are mispaired.

Polymerase uses 3 '→ 5' exonuclease activity to remove incorrect nucleotide.

Mismatch repair



A mismatch is detected in newly synthesized DNA.

The new DNA strand is cut, and the mispaired nucleotide and its neighbors are removed.

The missing patch is replaced with correct nucleotides by a DNA polymerase.

A DNA ligase seals the gap in the DNA backbone.

Source: Khan Academy