

# Lessons 9/10 Genes, DNA rules and DNA replication



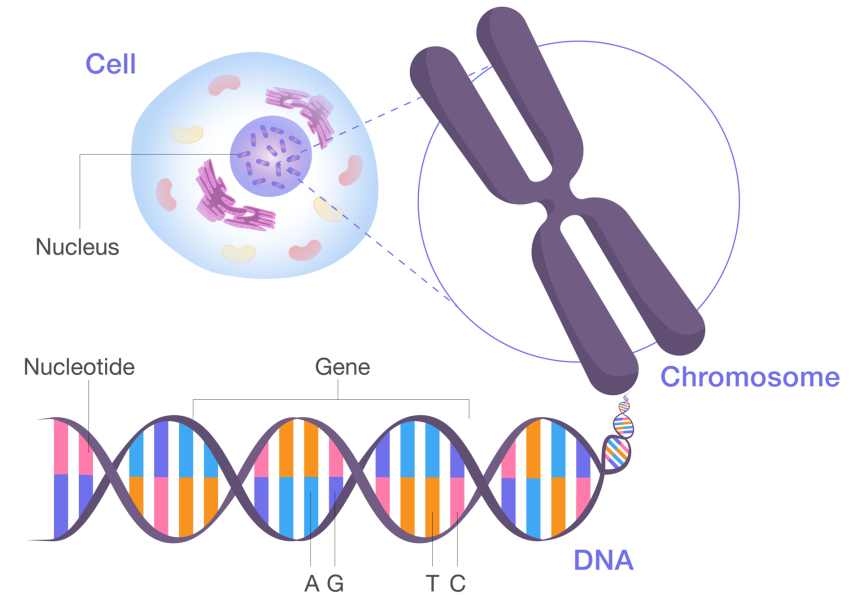
# Info transfer

- Information transfer in biology
  - key, crucial aspect of modern biology
- You need to know this material in order to understand anything at a higher level in biology



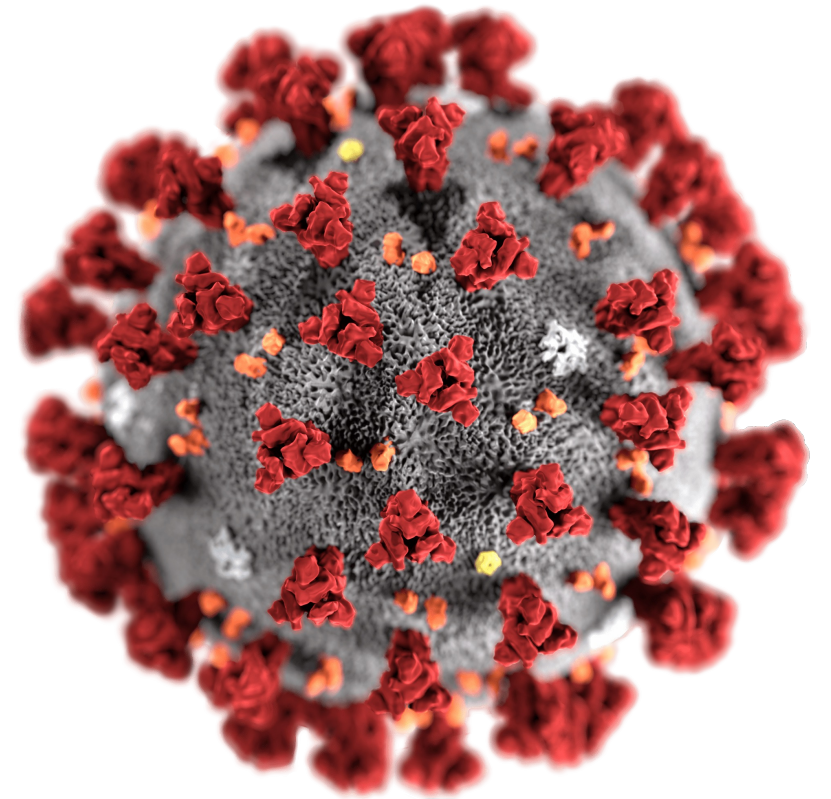
# Genes

- What is a **gene**?
- A piece of nucleic acid which contains all necessary instructions to generate a product (RNA or protein)



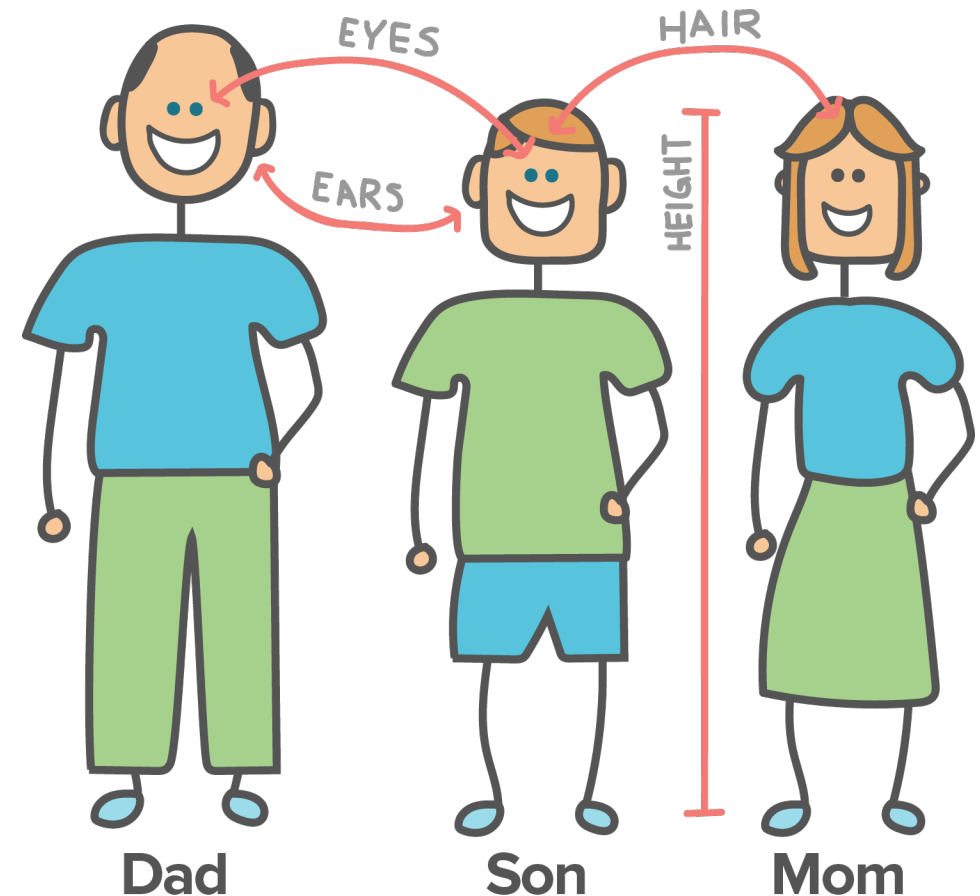
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- A piece of nucleic acid which contains all necessary instructions to generate a product (RNA or protein)
- Genes are usually DNA (but sometimes RNA, e.g., in RNA viruses like SARS-CoV-2)



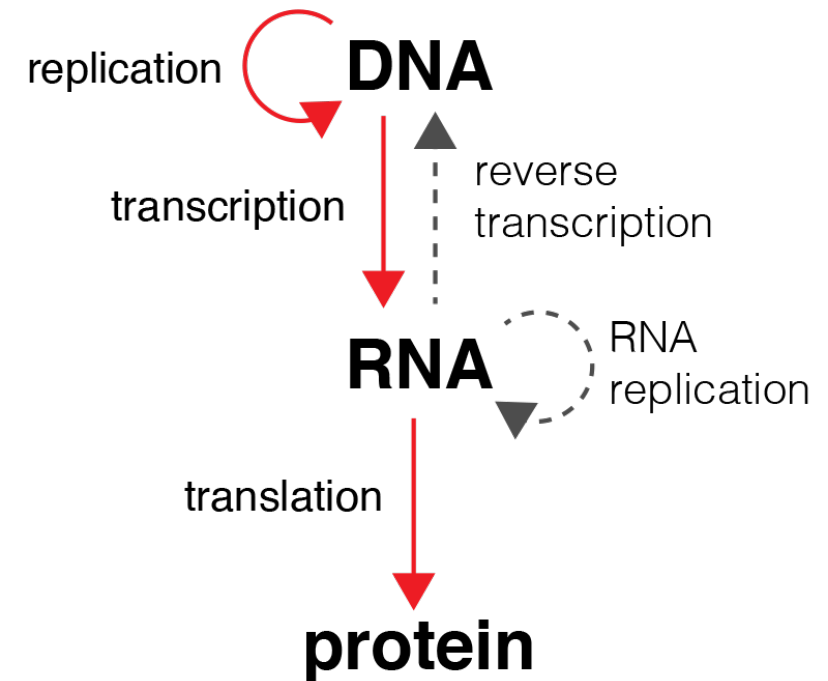
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- A piece of nucleic acid which contains all necessary instructions to generate a product (RNA or protein)
- Genes are usually DNA (but sometimes RNA, e.g., in RNA viruses like SARS-CoV-2)
- **Genes are the units of hereditary**

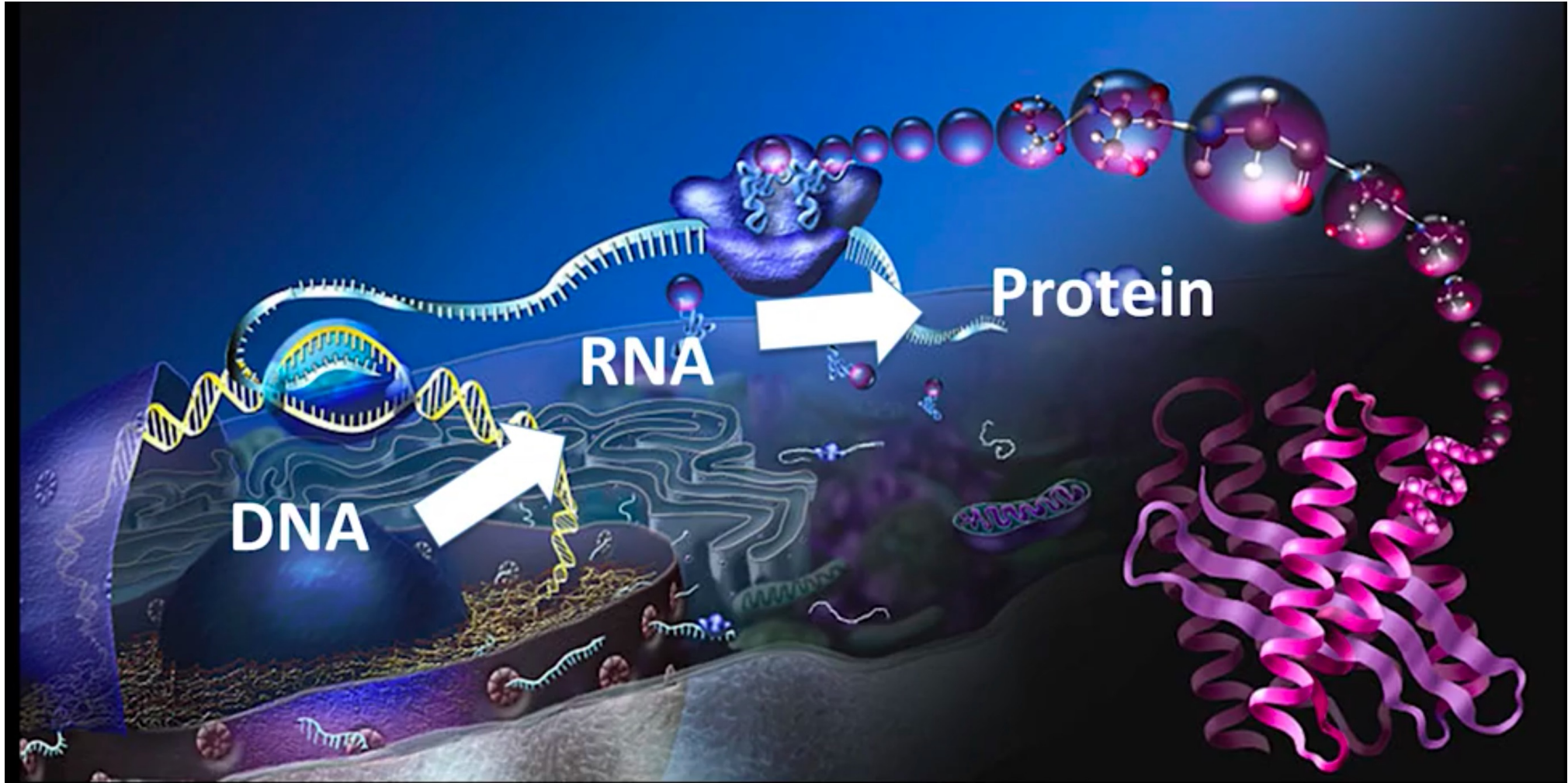


# Molecular biology and information transfer

- Molecular biology relies on information transfer
- The MB notion of information transfer:
  - **REPLICATION**: DNA (gene) replicates
  - **TRANSCRIPTION**: DNA is copied into RNA
  - **TRANSLATION**: RNA is translated into a protein
- This constitutes the **CENTRAL DOGMA OF MB** (already mentioned in Lesson 3)



# The MB central dogma (information transfer)



# DNA rules

- DNA base pairing rule
  - A makes **2 hydrogen bonds** with T
  - G makes **3 hydrogen bonds** with C
- Base pairing is associated with **complementary DNA strands**

A A T C  
T T A G



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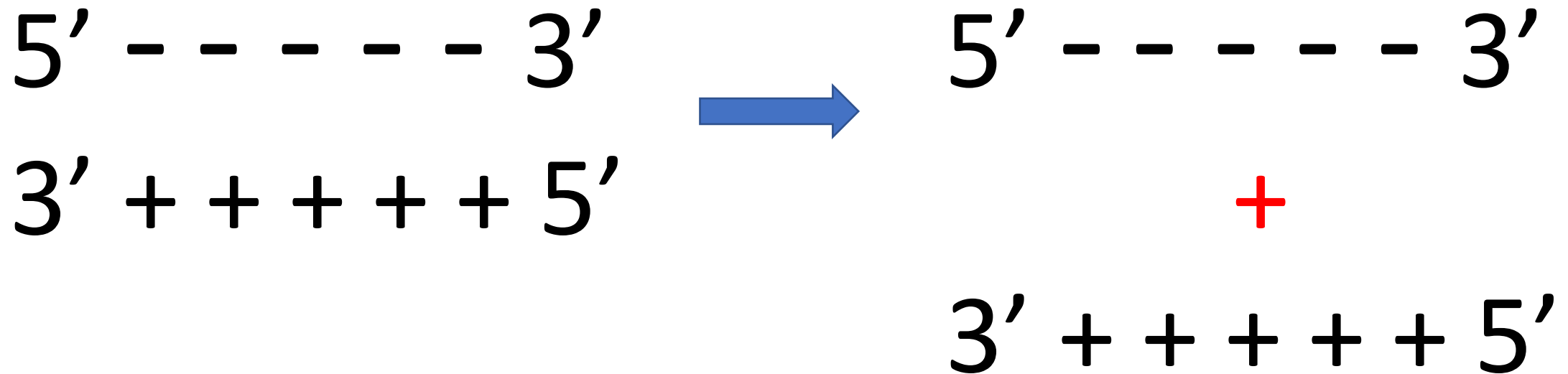
5' A A T C 3'  
3' T T A G 5'

# DNA replication

- **DNA replication** is a process that produces a DNA from a DNA template
- Takes place in the **cell nucleus**
- Mechanism by which genes (DNA) make more of themselves before they undergo cell division (mitosis or meiosis)

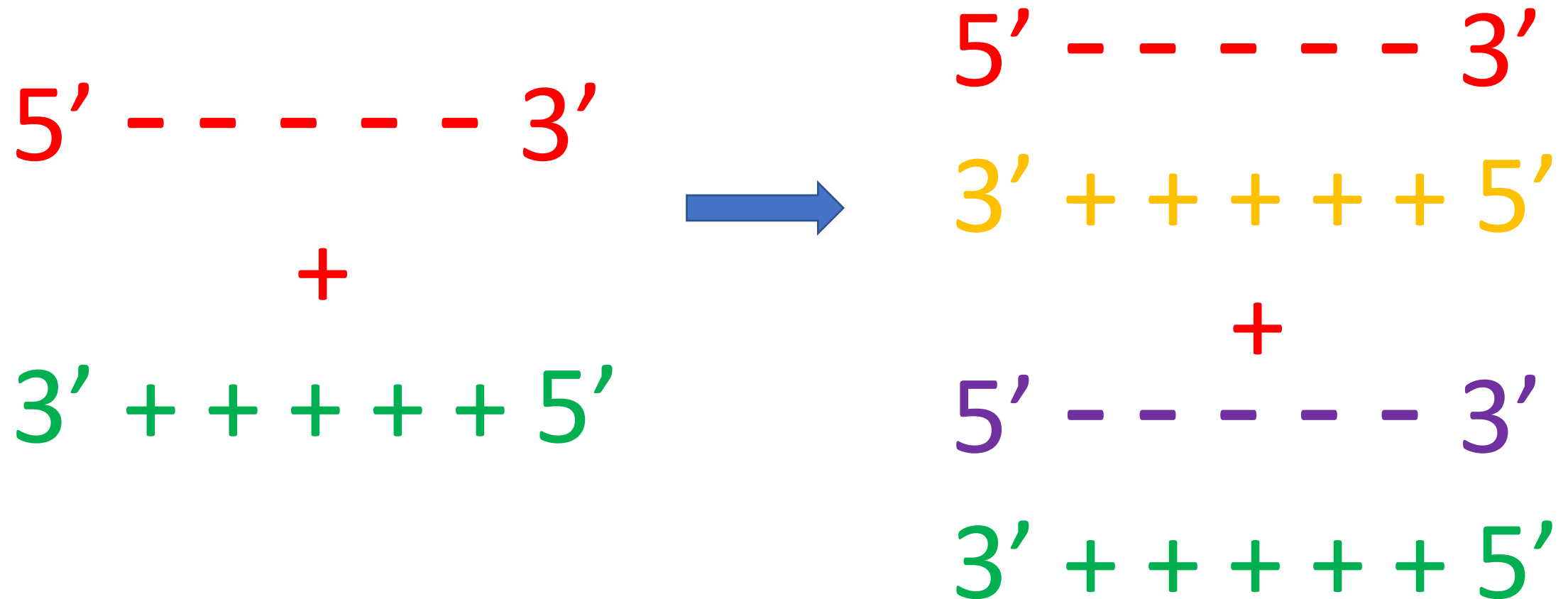
# DNA replication main stages

## 1. DNA strands separate



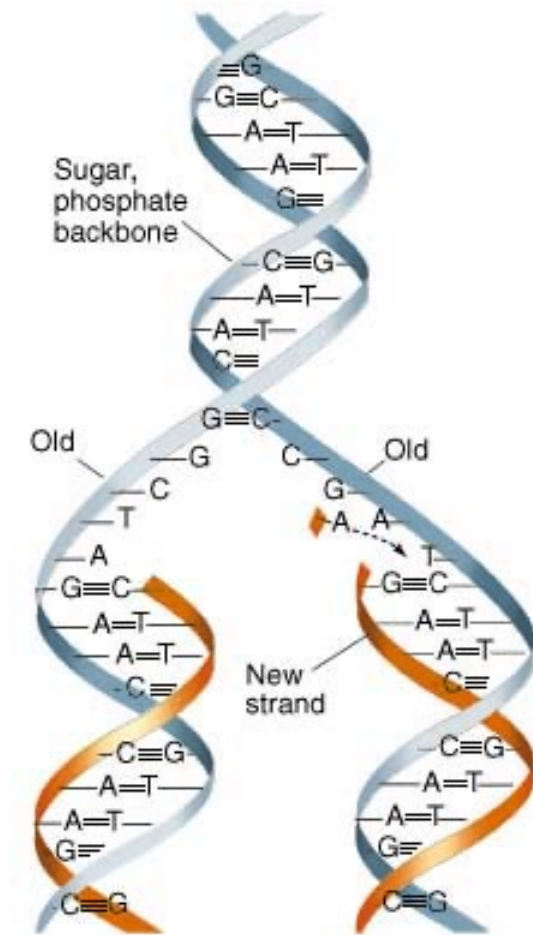
# DNA replication - a semiconservative process

2. Both strands are used as templates and copied



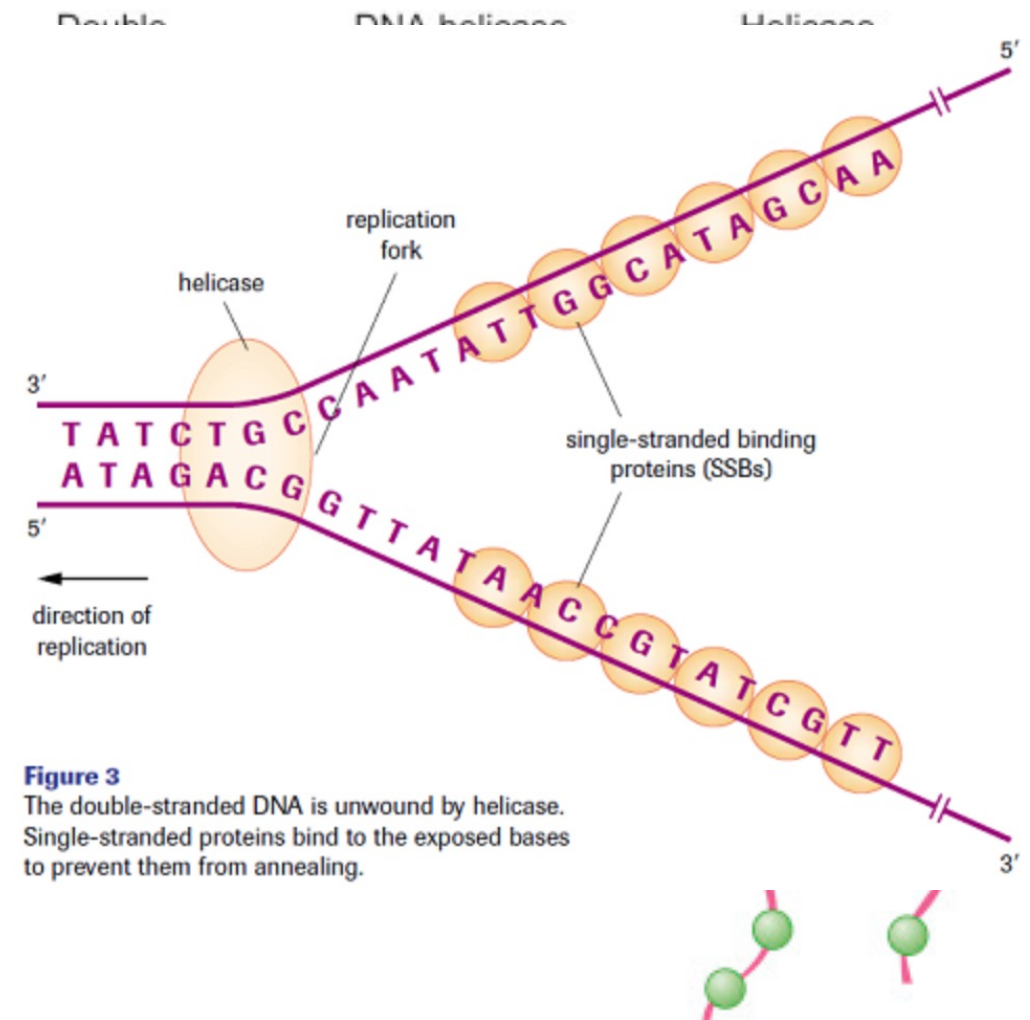
# DNA replication

- The process is absolutely dependent on the major DNA rule: **BASE PAIRING (BP)**
  - Only because of BP (complementarity) you can:
    - Take the two DNA strands apart
    - Fill them in
    - Come up with two new DNA molecules identical to the parent DNA
- **DNA replication occurs from each 3' end of each strand**
- **DNA replication requires a highly specialized and efficient crew**



# DNA replication – Unwinding the duplex

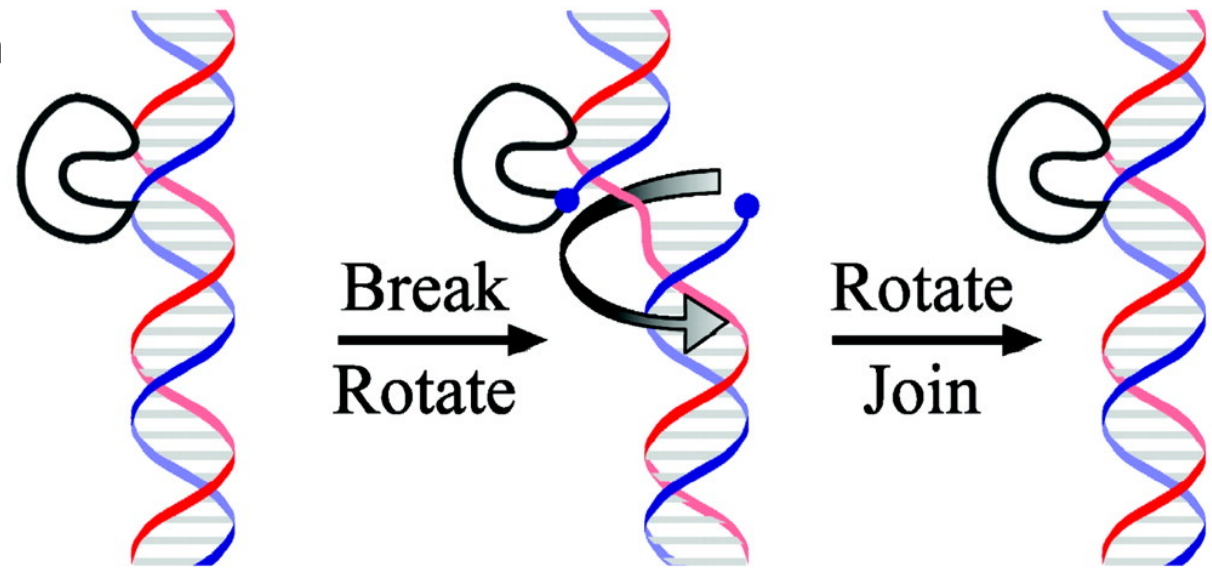
- The first step in DNA replication is DNA unwinding
  - This action is performed by enzymes called **helicases**
    - Unzip all H bonds leading to strand separation
- The second step is stabilizing the two single strands to prevent rejoining
  - This action is performed by a group of proteins called **single-strand DNA binding proteins (SSBPs)**



**Figure 3**  
The double-stranded DNA is unwound by helicase. Single-stranded proteins bind to the exposed bases to prevent them from annealing.

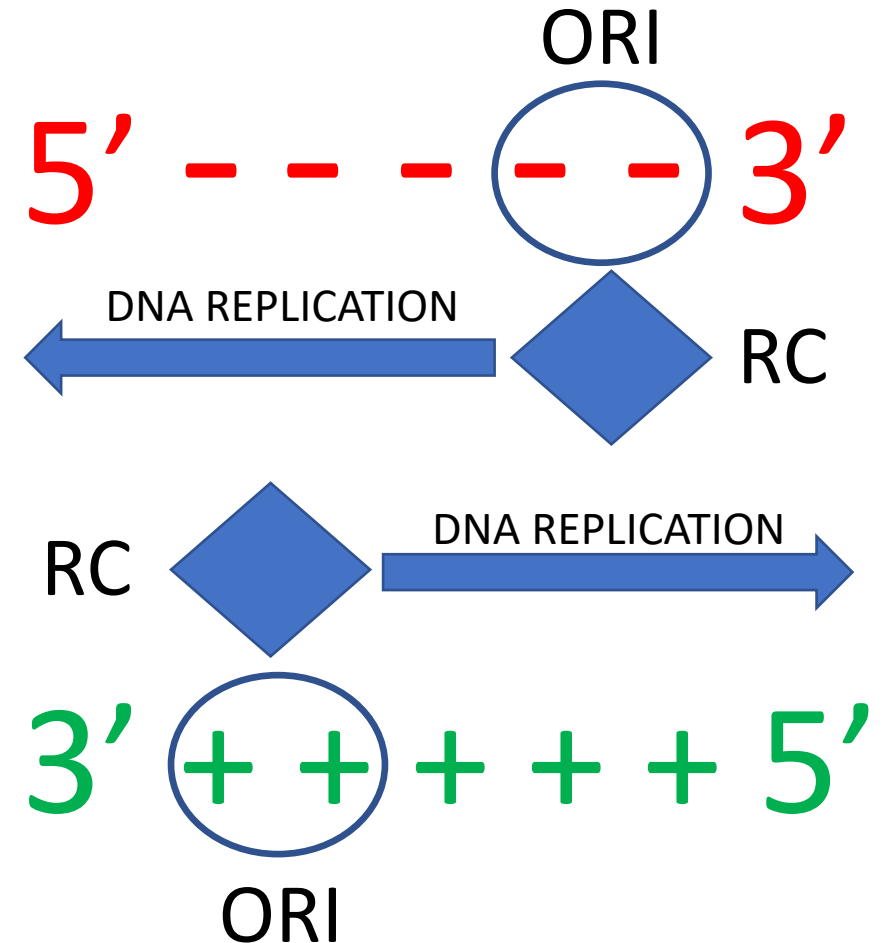
# DNA replication – Unwinding the duplex

- DH unwinding is more complex
  - The DNA DH is twisted
  - As it gets unzipped, these twists get pushed together, creating **tension** along the backbone
  - If not relaxed, the DNA backbone would become kinked preventing helicase from continuing its job
- Another enzyme, called **topoisomerase**, prevents this by:
  - Breaking backbone covalent bonds
  - Allowing for tension release
  - Resealing the DNA backbone



# DNA replication – it takes a lot more than two to tango

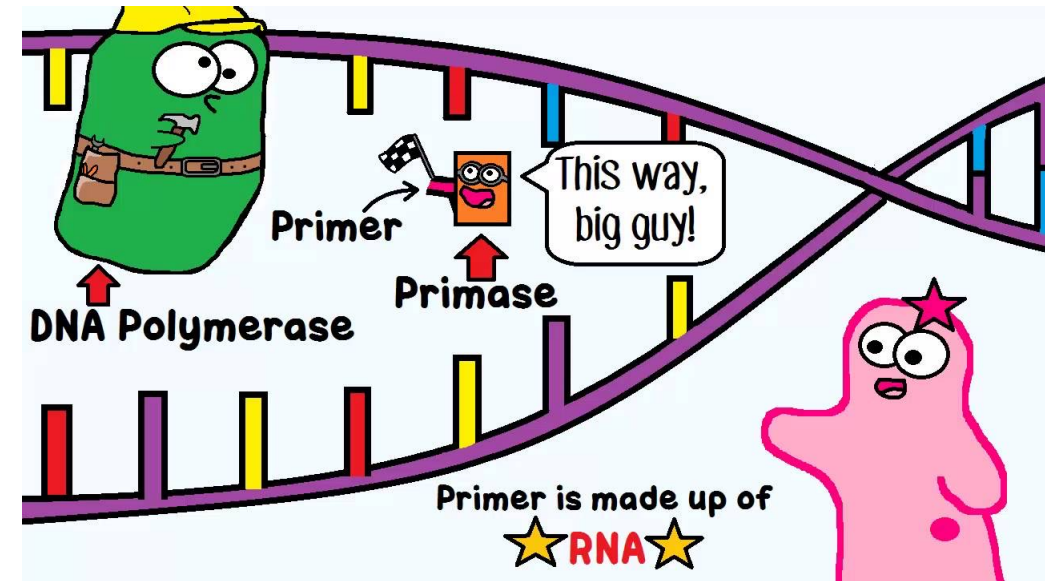
- DNA replication requires a “running start”
  - Specific nucleotide sequences within the chromosome called **origins of replication (ORI) (or DNA Primers)** where replication begins
    - There will be one ORI on each DNA strand
    - These are AT-rich sequences
  - A specific set of proteins recognizes the ORI and recruits other enzymes (**replication complex - RC**) to do the job
  - Replication occurs in both directions away from the ORI
    - Conducted by two enzyme complexes that move away from each other along the DNA





# DNA replication – Houston, we have a problem here....

- Within the RC, **DNA polymerase** is the enzyme that reads the code in the 3'-5' direction and build the new DNA strands
- **DNA POL cannot start replication on its own**
  - It can only add nucleotides to an existing strand!
  - It needs a helper enzyme to get the new strand started
- This helper enzyme is the **DNA primase**
  - An **RNA polymerase** that builds RNA strands and that can start a strand *per se*



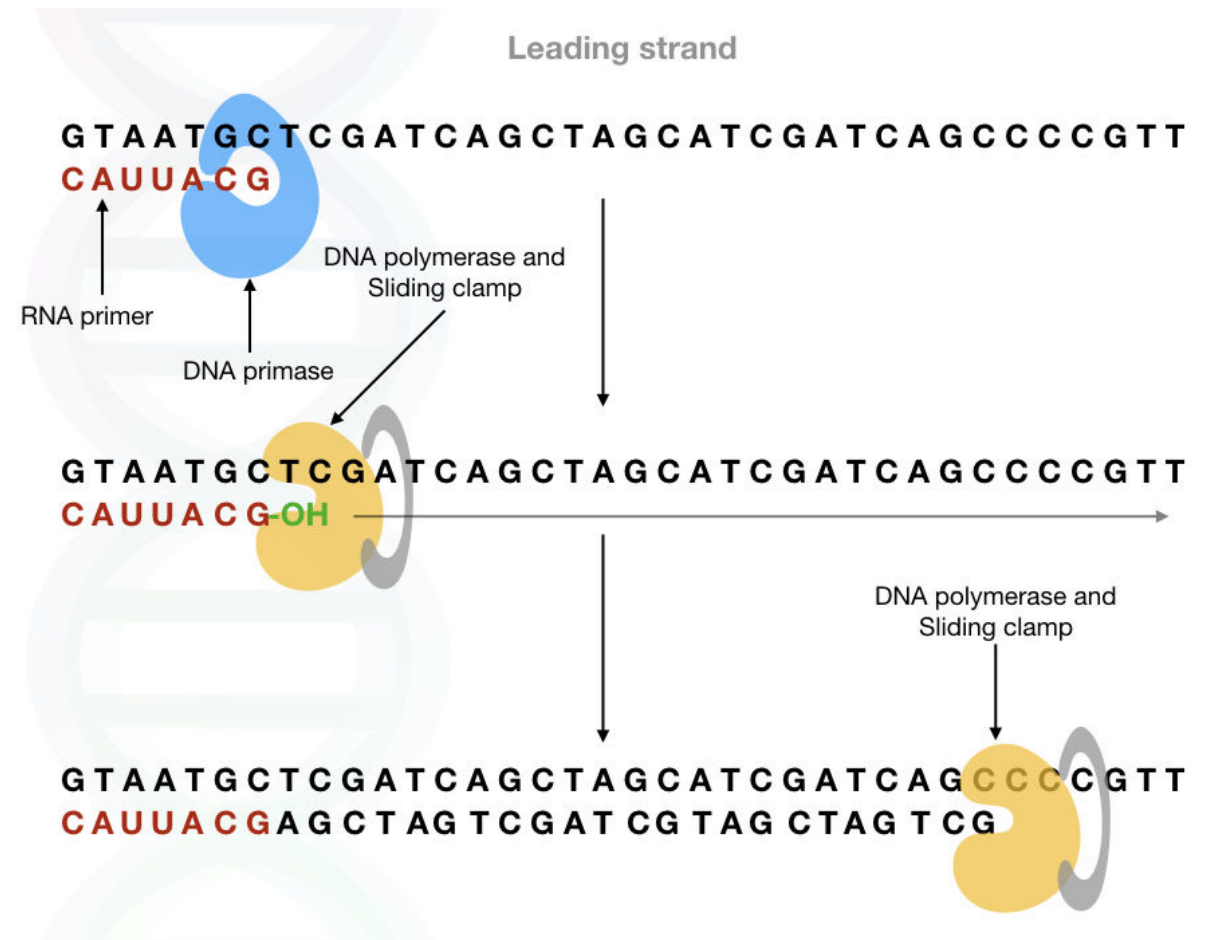
# DNA replication – DNA Primase to the rescue!

- The DNA primase
  - Synthesizes two short pieces of RNA (5-to-10 bp long) called **RNA primers**
    - These RNA primers are complementary to the ORIs (DNA primers) located on the two DNA strands
  - Attaches (**hybridizes**) the DNA and RNA primers via BP (complementarity)



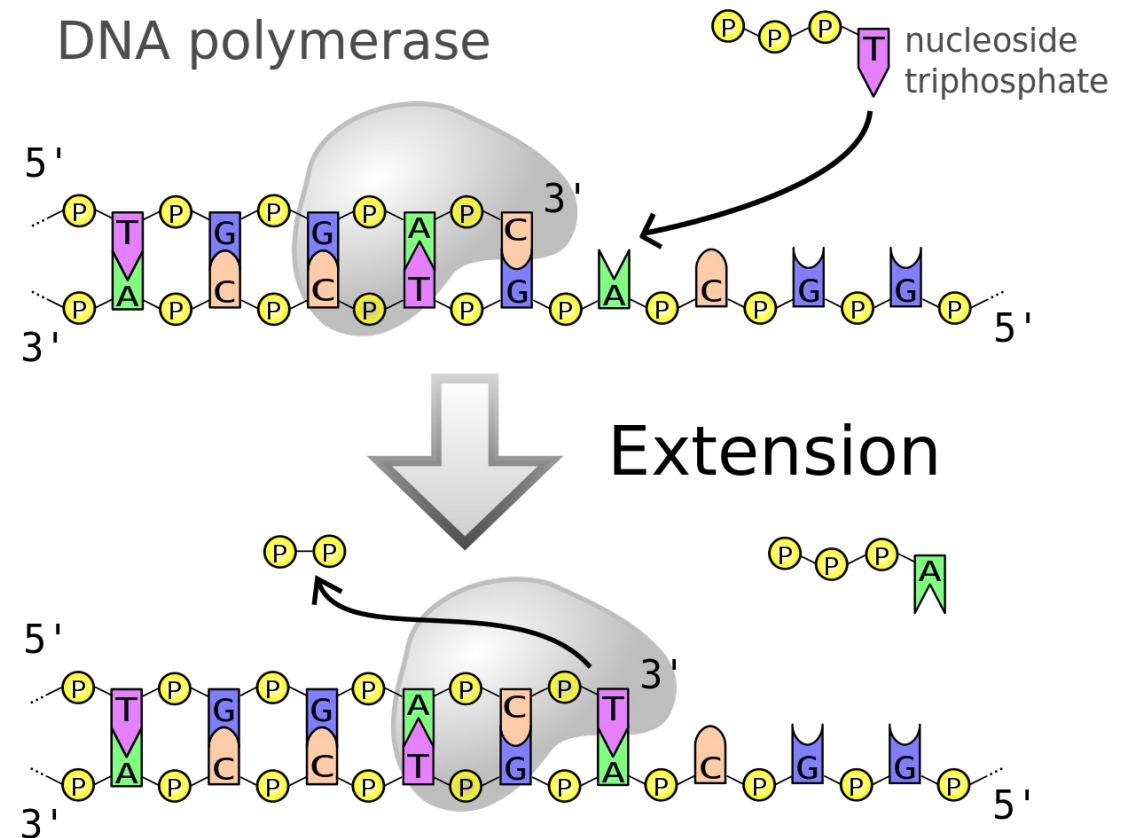
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- Once RNA primers are in place, DNA POL can start synthesizing DNA by attaching the correct nucleotides to the 3' ends of the primers (again via BP complementarity)



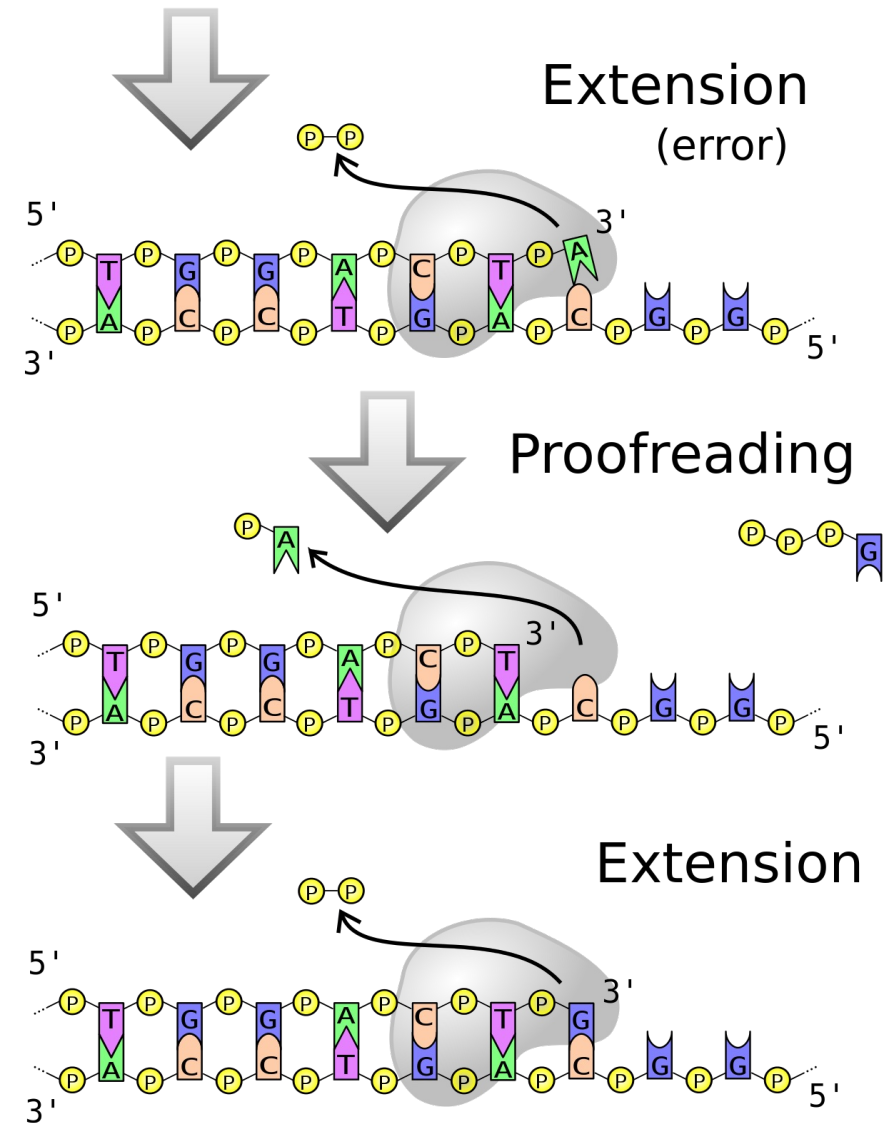
# DNA POL Proofreading

- During the DNA synthesis, DNA POL moves from 3' to 5'
  - The 5' end of the new nucleotide will be added to the 3' end of the growing chain
  - The new DNA strands grows in the 5' to 3' direction :)



# DNA POL Proofreading

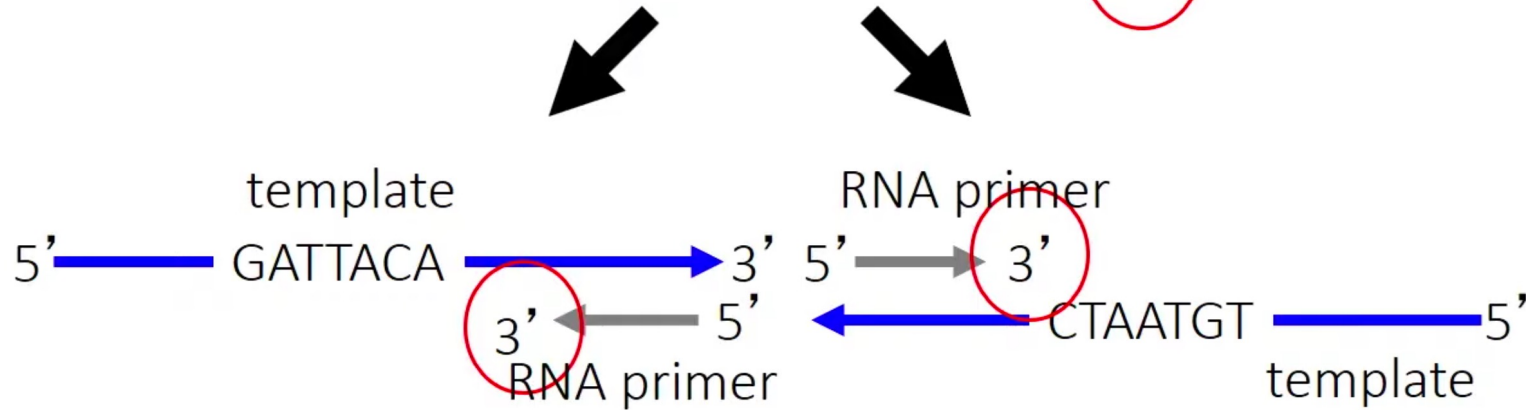
- DNA POL do make mistakes at a rate of about 1 per every 100,000 nucleotides
- That might not seem like much but
  - We humans have 6 billion base pairs in each diploid cell
    - that would amount to about 120,000 mistakes every time a cell divides
- DNA POL work is supervised by a **proofreading mechanism**



# DNA SEMICONSERVATIVE REPLICATION



strand separation, replication from each 3' end



replication of complementary strands

