

2.2 DNA POLYMERASE: THE KEY PLAYER

DNA polymerases are essential enzymes in DNA replication, which is the process of making copies of DNA. It catalyzes the formation of phosphodiester bonds during DNA replication. It does this by adding deoxynucleotide triphosphate (dNTP) to the growing polynucleotide chain, one nucleotide at a time. Each time the chain is elongated by one deoxyribonucleotide, a triphosphate molecule is released. Some DNA polymerases also check for errors in the DNA sequence and fix them using a process called proofreading, which involves removing and replacing any mistakes. DNA polymerases are grouped into seven families based on their similarities in sequence and structure. These families include those involved in DNA replication, repair, and even reverse transcription (Table below). The basic structure of all DNA polymerases consists of subdomains referred to as the **palm**, **fingers**, and **thumb** and resemble an open right hand. The palm contains catalytically essential amino acids in its active sites. The fingers are essential for nucleotide recognition and binding. The thumb is important for the binding of the DNA substrate. Between the finger and thumb domains is a pocket that is made up of two regions: the insertion site and postinsertion site. The incoming nucleotides bind to the insertion site and the new base pair resides in the postinsertion site. These subdomains, along with other subdomains specific to each family, are essential for the correct functioning of DNA polymerase. The structures of each of these subdomains are slightly different for each polymerase.

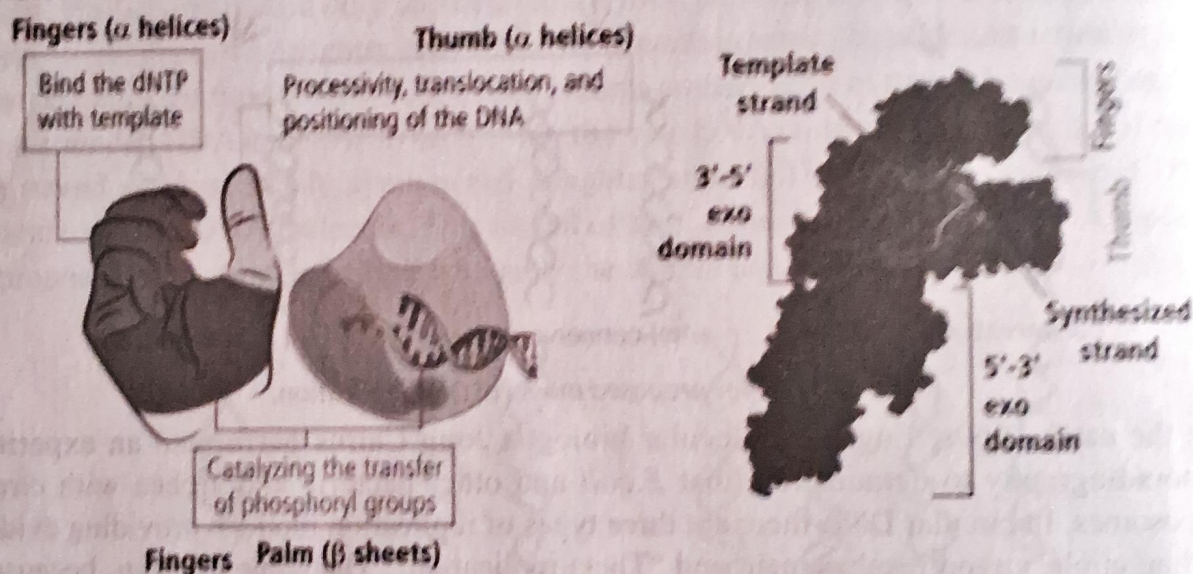


Fig. 2.3. Typical structure of a replicative DNA polymerase and its functional domains.

TABLE 2.1 Various families of DNA polymerases based on their structural domains.

Family	Function	Species	Examples
A	Replication and Repair	Eukaryotes and Prokaryotes	Pol I and Pol γ
B	Replication and Repair	Eukaryotes and Prokaryotes	Pol II, Pol α , Pol δ , and Pol ϵ
C	Replication	Prokaryotes	Pol III

D	Replication	Archaea	Unknown
X	Replication and Repair	Eukaryotes	Pol β , Pol μ , and Pol λ
Y	Replication and Repair	Eukaryotes and Prokaryotes	Pol IV, Pol V, Pol η , Pol κ , and Pol ι
RT	Replication and Repair	Eukaryotes, Viruses, and Retrovirus	Telomerase and Hepatitis B virus

While passing through several textbooks you may find various terminologies associated with DNA polymerases. In general DNA polymerase is abbreviated as DNA Pol or Dpo, if no other polymerase is being discussed only POL may also be used. Roman numerals or Greek letters are used to define subtypes e.g. POL I, Pol β etc. The name of organism or organelles may sometimes be used as prefix such as E. coli DNA polymerase may be abbreviated as EcDpo, or mitochondrial DNA polymerase as mtDpo. In the E. coli, the EcDpo III subunits β , γ , δ , δ' are named clamp loader. This complex assembles the β subunit sliding clamp onto the DNA. In eukaryotes, Dpo sliding clamp is made of the complex of Dpo and Proliferating Cell Nuclear Antigen (PCNA) which encircles it. Functional regions or domains in DNA polymerase may be named differently as per their functions, e.g. BRCT domain in Dpo is the C-terminal domain of breast cancer susceptibility protein. Klenow fragment is a large Dpo fragment produced upon cleavage of Dpo by subtilisin. As described in the table above there are several classes of DNA polymerases, yet we will discuss only key prokaryotic and Eukaryotic polymerases involved in replication here, considering the scope of this chapter.