DNA polymerases function in the replication and repair of chromosomes. Bacterial chromosome replication is performed by the replisome, a multi-subunit holoenzyme complex, comprised of a core polymerase complex (α, ε, δ), a clamp loader complex (ψ, β, γ, δ, ε, ψ), and a β-sliding clamp. A crystal structure of the DNA polymerase III α-subunit (Pollll) of *Thermus aquaticus* (Taq) with a template DNA fragment and a deoxyribozonucleotide has been recently determined. In the present project a physical model of Pollll was created. The Taq α-subunit has the similar "hand-like" structure of Pollll of *E. coli* and is composed of six subdomains: palm, fingers, thumb, histidinol phosphatase (PHP), β-binding, and a C-terminal domain (CTD). The catalytic palm domain is similar to the eukaryotic DNA repair polymerase, Polβ, and not eukaryotic replicative DNA polymerases. Three highly conserved aspartate residues (D463, D465, D618) within the palm domain coordinate divalent metals involved in catalysis. A conserved glycine-serine motif (G425, S426) and four conserved arginine residues (R452, R455, R766, R767) participate in incoming nucleotide binding. A lysine residue (K616) near the catalytic site positions the 3′-terminal phosphate of the primer strand for dNTP addition. Incoming nucleotides undergo deoxyribose selection and pre-catalytic positioning in an entry channel through the fingers domain. Upon binding DNA, the α-subunit undergoes a conformational shift allowing interactions with the sugar-phosphate backbone. Several subdomains contribute to forming a DNA binding pocket. Interaction of a loop from the β-binding site with a cleft within the β-clamp supports a model for polymerase switching.

**Abstract**

DNA polymerases are molecular complexes crucial for maintenance of DNA through multiple functions including editing, repair, and replication. This model displays the α-subunit crystal structure of *Thermus aquaticus* DNA polymerase III (Taq Pollll). There are six families of DNA-dependent DNA polymerases (Bailey et al., 2006; Wing et al., 2008). Family C, to which Taq Pollll belongs, and family X make up the Pollll-like nucleotidytransferase superfamily characterized by the structure of the palm domain's catalytic site (Lamers et al., 2006). All polymerases, regardless of family, use the same catalytic mechanisms despite structural differences. The most thorough method to observe relationships between structure and functions is through X-ray crystallography of a ternary complex which includes enzyme, DNA, and incoming NTP. The structurally similar *E. coli* Pollll subunit has been crystallized; however, the protein is truncated as well as lacking DNA and NTP (Lamers et al., 2006). The ternary complex for observing DNA-influenced conformational changes. These observations, along with other structural comparisons, give insight into evolutionary lineage.

**Introduction**

DNA polymerases are molecular complexes crucial for maintenance of DNA through multiple functions including editing, repair, and replication. This model displays the α-subunit crystal structure of *Thermus aquaticus* DNA polymerase III (Taq Pollll). There are six families of DNA-dependent DNA polymerases (Bailey et al., 2006; Wing et al., 2008). Family C, to which Taq Pollll belongs, and family X make up the Pollll-like nucleotidy- transferase superfamily characterized by the structure of the palm domain's catalytic site (Lamers et al., 2006). All polymerases, regardless of family, use the same catalytic mechanisms despite structural differences. The most thorough method to observe relationships between structure and functions is through X-ray crystallography of a ternary complex which includes enzyme, DNA, and incoming NTP. The structurally similar *E. coli* Pollll subunit has been crystallized; however, the protein is truncated as well as lacking DNA and NTP (Lamers et al., 2006). The ternary complex for observing DNA-influenced conformational changes. These observations, along with other structural comparisons, give insight into evolutionary lineage.

**Summary**

- A model of *T. aquaticus* DNA Pollll was created. This is the first crystallized structure of a ternary complex including enzyme, DNA, and an incoming nucleotide.
- The homology of this enzyme with eukaryotic DNA Polβ, a DNA repair polymerase, shows that *T. aquaticus* and *E. coli* Pollll, a replicative polymerase, may possibly share an evolutionary link. This concept is contrary to the prior hypotheses in which eukaryotic and bacterial replicative enzymes share an ancestral lineage.
- Future research will include a resource page (Proteopedia.com) and possibly creation of more molecular models once future crystallizations of the entire DNA replication holoenzyme or replisome complex become available.

**References**


**PDB Files**

Model: 3EDD - *T. aquaticus* DNA polymerase III α (ternary complex)
Image: 2HDA - *E. coli* Pollll
Image: 2HPI - *T. aquaticus* Pollll (uncomplexed)
Image: 1BPD - *Rattus norvegicus* Pollll

* The CREST Program is funded by grant #1027279 from NSF-CCLI.