Lec. 4 Biomedical 3rd year

DNA polymerase processivity

Not only does DNA polymerase catalyze phosphodiester bond formation, but it also does so repeatedly. Indeed, the same DNA polymerase molecule successively attaches one nucleotide after another to the growing daughter strand much faster than it dissociates from the DNA. This property of remaining attached to the DNA through many rounds of nucleotide addition is referred to as **processivity**. Processivity maximizes the speed of DNA synthesis. If the polymerase frequently fell off the DNA and had to re-bind in order to resume nucleotide incorporation, the rate of DNA synthesis would be much slower.

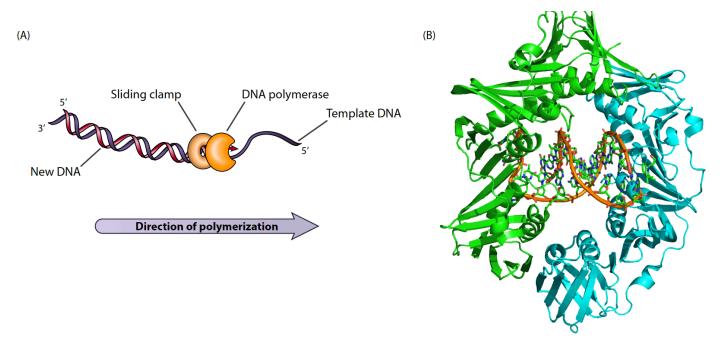


Figure 11 The sliding clamp allows DNA polymerase to be processive

<u>What keeps the enzyme anchored to the DNA?</u> The answer is geometrically elegant and simple: DNA polymerase is tethered to the DNA by a <u>sliding clamp</u> that fully encircles the DNA helix (Figure 11A). The sliding clamp is a complex of proteins that forms a complete circle around the DNA. In effect, it resembles a doughnut, with the DNA passing through the hole in the doughnut. The sliding clamp slides on the DNA along with the DNA polymerase to which it is attached and travels with it as DNA synthesis proceeds. Thus, the sliding clamp tethers the polymerase to the DNA by means of a topologically closed structure. The beautiful X-ray

structure of the clamp in Figure 11B shows how the hole in the doughnut accommodates the DNA.

DNA Major and Minor Grooves:

The direction in nucleic acids is specified by "referring to the carbons of the ribose ring in the sugar-phosphate backbone of DNA. The 5' symbol specifies the 5th carbon in the ribose ring, while, the 3' specifies the 3rd carbon atom in the ribose ring.

So when the nucleotides stack upon each other we get alternating larger angle (Larger face) - Major grove and small angle (Smaller face) - Minor grove on the double helix. (Figures below) A single turn of the helix constitutes about ten nucleotides, and contains a major groove and minor groove, the major groove being wider than the minor groove.

The major and minor grooves are opposite each other, and each runs continuously along the entire length of the DNA molecule. These turns arise from the antiparallel arrangement of the two backbone strands. The major groove, is 22 Å wide, it is deep and wide. As a result, proteins such as <u>transcription factors</u> that can bind to specific sequences in double-stranded DNA usually make contact with the sides of the bases exposed in the major groove. The minor groove on the other hand, is 12 Å wide, it is narrow and shallow. The width of the major groove makes it more accessible to the proteins than in the minor groove which is essential to the cell life because these interactions include the processes of (<u>DNA replication transcription activation, repression and</u>



