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18/MHS07/021

PHARMACOLOGY

BCH 204 ASSIGNMENT

QUESTION

1. Highlight the steps of DNA replication
2. Outline the functions of DNA replication enzymes
3. Steps of DNA replication

Basics of replication

Replication depends on the pairing of bases between the two strands of DNA. The A base can only bind to a T, and a C can only bind to a G. In the DNA double helix, the bases of one strand face across and bind to those of the other strand. Therefore, the base sequence of each strand complements that of the other -- the sequences are antiparallel and serve as templates for each other’s replication. The two strands are labelled by the location of certain chemical bonds in the DNA backbone. The cell can replicate the “leading strand" as a single unit, but must replicate the “lagging strand" in small pieces.

There are 3 main steps of DNA replication. They are;

## Initiation

Replication begins at a location on the double helix known as “oriC” to which certain initiator proteins bind and trigger unwinding. Enzymes known as helicases unwind the double helix by breaking the hydrogen bonds between complementary base pairs, while other proteins keep the single strands from rejoining. The “topoisomerase” proteins surround the unzipping strands and relax the twisting that might damage the unwinding DNA. The cell prepares for the next step, elongation, by creating short sequences of RNA called primers that provide a starting point of elongation.

## Elongation

With the primer as the starting point for the leading strand, a new DNA strand grows one base at a time. The existing strand is a template for the new strand. For example, if the next base on the existing strand is an A, the new strand receives a T. The enzyme DNA polymerase controls elongation, which can occur only in the leading direction. The lagging strand unwinds in small sections that DNA polymerase replicates in the leading direction. The resulting small “Okazaki fragments” can contain 1,000 to 2,000 bases in bacteria, but eukaryotes -- organisms having cells with nuclei -- have fragments of only 100 to 200 bases. The fragments terminate in an RNA primer that is subsequently removed so that enzymes can stitch the fragments into an elongating strand.

## Termination

After elongation is complete, two new double helices have replaced the original helix. During termination, the last primer sequence must be removed from the end of the lagging strand. This last portion of the lagging strand is the telomere section, containing a repeating non-coding sequence of bases. Enzymes snip off a telomere at the end of each replication, leading to shorter strands after each cycle. Finally, enzymes called nucleases “proofread” the new double helix structures and remove mispaired bases. DNA polymerase then fills in the gaps created by the excised bases.

1. Functions of DNA replication enzymes
2. **DNA Helicase**

Unwinds the DNA double helix at the replicating forks

1. **Gyrase**

Relieves the build-up of torque during unwinding

1. **DNA Primase**

Lays down RNA primers

1. **DNA polymerase III**

Main DNA synthesis enzyme

1. **DNA polymerase I**

Replaces RNA primers with DNA

1. **DNA Ligase**

Fills in the gaps. Re-joins the two DNA strands into a double helix and joins Okazaki fragments of the lagging strand

1. Topoisomerase

Relaxes the super- coiled DNA