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**Assignment**

1. Highlight the steps of DNA Replication
2. Outline the functions of DNA Replication enzymes

**Answer**

1. **Steps of DNA Replication**

DNA replication is the process by which DNA makes a copy of itself during cell division. There are three main steps to DNA replication: *initiation, elongation, and termination.*

1. **Initiation**

The DNA synthesis is initiated at certain points within the DNA strand known as ‘origins’, which are the specific coding regions. These origins are targeted by various initiator proteins, which go on to recruit more proteins that help the replication/Duplication process, forming a replication complex around the DNA’s origin. There are several origin sites, and when replication of DNA begins, these sites are referred to as Replication Forks. Within the replication complex is an enzyme DNA Helicase, which unwinds the double helix and exposes each of the two strands, so that they can be used as a template for replication. This is done by hydrolysing the ATP used to form the bonds between the nucleobases, therefore breaking the bond between the two existing strands.

The DNA can only be extended by the addition of a free nucleotide triphosphate to the 3’- end of a chain. As the double helix runs antiparallel, but DNA replication only occurs in a specific direction, it means growth of the two new strands is very different, as both will be covered in Elongation. DNA Primase is also another enzyme that is important in DNA replication. It synthesises a small RNA primer, which starts the reaction for DNA Polymerase. DNA Polymerase is the enzyme that is ultimately responsible for the making and expansion of the new strands of DNA.

1. **Elongation**

Once the DNA Polymerase is attached to the original, unzipped two strands of DNA (e.g. the template strands), it has the ability to start synthesising the new DNA to match the templates. This enzyme can only extend the primer by adding free nucleotides to the 3’-end of the strand, causing difficulty as one of the template strands has a 5’-end from which it needs to extend from. One of the templates is read in a 3’ to 5’ direction, which means that the new strand that will be formed, will be formed in a 5’ to 3’ direction, due to the fact that the two strands are antiparallel to each other. The newly formed strand is referred to as the Leading Strand. Along this strand, DNA Primase only needs to synthesise an RNA primer once, at the beginning, to help initiate DNA Polymerase to continue extending the new DNA strand. This is because DNA Polymerase is able to extend the new DNA strand normally, by adding new nucleotides to the 3’ end of the new strand.

However, the other template strand is antiparallel, and is therefore read in a 5’ to 3’ direction, meaning the new DNA strand formed will run in a 3’ to 5’ direction. This now becomes an issue, as DNA Polymerase doesn’t extend in this direction. To counter this, DNA Primase synthesises a new RNA primer approximately every 200 nucleotides, to prime DNA synthesis to continue extending from the 5’ end of the new strand. To allow the continued making of RNA primers, the new synthesis is delayed and as such, called the Lagging Strand.

The leading strand is a complete strand, while the lagging strand is incomplete. It is instead made out of numerous ‘mini-strands’, known of Okazaki fragments. These fragments occur due to the fact that new primers are having to be synthesised, therefore causing multiple strands to be created, which is different from the one initial primer that is used with the leading strand.

1. **Termination**

The process of expanding the new DNA strands is continued until there is either no other DNA template left to replicate (e.g. at the end of the chromosome), or two replication forks meet and eventually terminate. The meeting of two replication forks is not structured and happens randomly along the course of the chromosome. Once DNA synthesis has finished, it is also important that the newly synthesised strands are bound and stabilized. With regards to the lagging strand, two enzymes are needed to achieve this; RNA polymerase H removes the RNA primer that is located at the beginning of each Okazaki fragment, and DNA Ligase joins two fragments together forming one complete strand. Now with two new strands finally finished, the DNA has successfully been replicated, and will just need other intrinsic cell systems to ‘proof-read’ the new DNA to check for any errors in replication process, and for the new single strands to be stabilized.

1. **Functions of DNA Replication Enzymes**
* **Topoisomerase:** Relaxes the super-coiled DNA.
* **DNA helicase:** Unwinds the double helix at the replication fork.
* **Primase:** Provides the starting point for DNA polymerase to begin synthesis of the new strand.
* **DNA polymerase:** Synthesizes the new DNA strand; also proofreads and corrects some errors.
* **DNA ligase:** Re-joins the two DNA strands into a double helix and joins Okazaki fragments of the lagging strand.