Replication

Process of DNA replication

- **Origin of replication**
- **Most of eukaryotic DNAs have multiple origins of replication.**
- **Prokaryotes have only one origin**
- **oric C(*E.coli*) present within a 245 bp region**
- **This region has three repeats of a 13bp long sequence (GATCTNTTNTTTT) and 4 repeats of a 9bp sequence (TTATNCANA).**
- **The origin of replication in a number of plasmids and phages are also present.**
- **In general, the sequences at the origin of replication are A:T rich, which makes the melting of dsDNA easier.**

Process of DNA replication

- **Origin of replication in yeast is ARS.**
- **The origin from higher organisms have not been well identified.**
- **To initiate the DNA replication a protein factor, DnaA recognizes and binds at the origin of replication.**
- **The binding of DnaA is with the repeat of Oric C.**
- **The binding of DNaA is preceded by the binding of small stretch of DNA. This region of DNA opens up to form a single stranded region and the separation of two strands takes place. This structure is referred as replication fork.**

Process of DNA replication

- **The single stranded character of replication fork is maintained by the binding of single strand binding protein as SSB proteins.**
- **The association of these proteins prevent the formation of dsDNA.**
- **Another ancillary protein cause the activation of primase which synthesize the RNA primer. The primer is complementary to 3^{l} end of the template.**
- **The activity of DnaB is facilitated by the binding of another protein, DnaC to DnaB.**
- **Once the primer has initiated the DNA synthesis, DNA polymerase takes over and adds more nucleotides one at a time to initiate replication. The entire complex is referred as primosome.**

Process of DNA replication

- **once initiation has taken place and the DNA synthesis continues.**
- **The primosome can move along the SSDNA.**
- **During the entire process the helicase keeps binding ahead of the fork so that there is a forward movement of the fork.**
- **The elongation of the chain is relatively simple process.**
- **The new nucleotide ancillary factor complex of a growing chain is referred as the replisome.**

Leading and Lagging Strands

- **The synthesis of template which will be copied in the 5/-3/ direction by DNA polymerase.**
- **The synthesis of other strand(5/-3/ of template) which apparently seems to grow in 3/-5/ direction takes place. The problem was solved in 1960s.**
- **Reiji Okazaki and his colleagues discovered the presence of a large number of small DNA fragments, each with an RNA primer attached to it, in the dividing cells.**
- **It has been now well established that the synthesis of this strand also takes place only in the 5/-3/ direction.**
- **The primase initiate the synthesis of DNA at the 3/ end of opened region of fork and polymerase extended this towards 5/ side synthesizing new DNA in 5/-3/ direction.**
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Leading and Lagging Strands

- When more bases of DNA template open up and the size of the fork is increased, a new primer is synthesized and gets annealed at the 5/ of the fork and entire process is repeated until the polymerase has reached to the first primer.
- The 5/-3/ exonuclease activity of Pol I at this digest the RNA primer and the polymerase fills the gap with DNA
- Thus synthesis of this strand takes place in pieces.
- DNA ligase join to form continuous DNA strand.
- There are separate primases for leading and lagging strands.
- One strand is known is leading strand(continuous)
- other lagging strands(discontinuous).
- simple primosome formation for leading strand
- multiple primosomes for lagging strand.

Leading and Lagging Strands

- **Each primosome results in the formation of a single Okazaki fragment.**
- **This replication takes place only if two separate DMA polymerase molecules are involved in replication of leading and lagging strands.**
- **Holoenzyme Pol III is made up of two catalytic cores.**
- **one of the core of same molecules catalyses the replication of leading strand while other catalyses the replication of lagging strand.**