Thinking exercise

DNA synthesis is carried out by a group of proteins that act together as a replication machine. Some human diseases are associated with defects in some aspect of this "machine." For each of the following scenarios, determine in which protein or proteins you would be most likely to find a defect based on the observation. What is your reasoning? You can pair with another student to discuss your hypotheses.

Observed defect:	Protein(s) likely involved:
1. Bloom's Syndrome patients are small in size, have impaired immunity, and develop cancer earlier than the general population. If one were to re-create a replication fork from these patients *in vitro*, the formation of single-stranded DNA would be much slower than in the general population.	
2. In some tumors, the number of mutations after a round of replication is significantly higher than the mutation rate seen in normal tissue.	
3. In cells observed in a lab, the replication fork can form, but no new DNA is synthesized on either leading or lagging strands.	
4. In cells observed in a lab, the okazaki fragments are not joined	

Multiple choice questions

1. What are identifying features of a DNA-only transposon?
    a. Long terminal repeats at each end
    b. Reverse transcriptase and endonuclease as specialized enzyme
    c. Transposase as specialized enzyme
    d. no RNA intermediate
    e. Short inverted repeats at each end

2. How is negative selection defined and identified?
    a. By a decreased amount of mutations in certain parts of the genome
    b. By an accelerated mutation rate in certain parts of the genome
    c. By comparing different ancestors and their gene similarity
    d. Negative selection only occurs in Introns

3. How is it possible to follow the evolution of a single gene?
    a. By comparing the gene to those of the common ancestor
    b. By looking for orthologues/paralogues
    c. By looking for the gene in an unrelated organism

   d. By looking at the folding of the protein that is made from this gene

4. What is the order in which the enzymes need to act for successful DNA replication

   a. DNA Helicase – DNA Primase – DNA Polymerase – DNA Ligase
   b. DNA Primase – DNA Helicase – DNA Polymerase – DNA Ligase
   c. DNA Ligase – DNA Helicase – DNA Primase – DNA Polymerase
   d. DNA Polymerase – DNA Ligase – DNA Helicase – DNA Primase

5. What is correct when we study the synthesis of the lagging strand?
   a. DNA Polymerase synthesizes in 3'-5' direction
   b. There is no activity from the DNA ligase
   c. DNA Polymerase runs in the RNA primer and falls off, leaving a gap
   d. There is a ligase activity needed
   e. All of the above

6. Since the first nucleotides cannot be linked in a newly synthesized strand in DNA replication, _____ is required.
   a. SSB proteins binding DNA
   b. an RNA primer
   c. DNA Helicase
   d. a DNA primer
   e. DNA polymerase

7. Okazaki fragments are used to elongate
   a. both strands in both directions
   b. the lagging strand toward the replication fork
   c. the leading strand away from the replication fork
   d. the lagging strand away from the replication fork
   e. the leading strand toward the replication fork

TRUE or FALSE

1. 50 % of the human genome are made up by repeated sequences

   TRUE or FALSE

2. Transposon libraries are used to assess the importance of each gene under a certain condition.

   TRUE or FALSE

3. Analogues are similar genes in different genomes derived from a common ancestor

   TRUE or FALSE

4. During replication, two identical replicas of DNA are made from one original DNA molecule

   TRUE or FALSE

5. Loading of the sliding clamp is done once and it remains associated to the DNA strand until replication is completed

   TRUE or FALSE

6. Okazaki fragments remain during replication and lead to breakage of the DNA in the lagging strand.

   TRUE or FALSE

7. Both leading and lagging strand are replicated discontinuously

   TRUE or FALSE