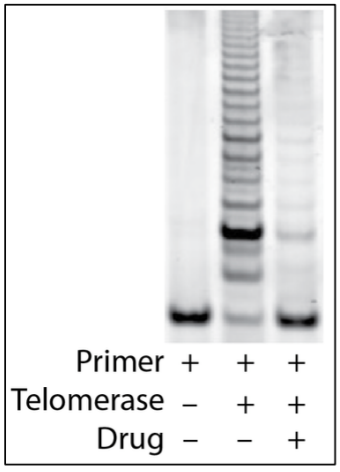
Question 2 – DNA Replication and DNA repair (25 pts).

2.1 Do the following statements apply to Bacteria, Eukaryotes, Both Bacteria and Eukaryotes, or Neither Bacteria nor Eukaryotes?
Write "Bacteria", "Eukaryotes", "Both", or "Neither" as appropriate in the boxes below (1.5 pts each).

	Incomplete transcripts are used as emergency primers to restart DNA replication.
	Polymerases synthesize DNA in the 3' to 5' direction on the lagging strand.
	The leading and lagging strand are synthesized by different polymerases.
	Sliding clamps are used to increase processivity in lagging strand synthesis.
	DNA replication proceeds bidirectionally from a single origin site.
	Sliding clamps are loaded onto RNA:DNA hybrids by clamp loader complexes.
	The reverse transcriptase activity of telomerase extends chromosome 3' ends.
	DNA methylation is used to distinguish old from new DNA in mismatch repair.
	Nucleosomes are removed from DNA behind the replication fork.
	Initiation of DNA replication requires the melting of double-stranded DNA.

2.2-2.4: Scientists are trying to understand the mechanism of action of a new drug that shows promise as an anticancer agent. They discover that this drug directly impacts telomerase, which they assessed by measuring the ability of purified human telomerase to extend a 24 nt-long telomeric repeat primer in the presence (+) and absence (-) of the drug, with the products assessed using autoradiography. The results are shown on the right.



2.2: What are the bands that appear upon the addition of telomerase to the reaction? Justify your answer briefly (3 pts).

2.3: What is the impact of the drug on telomerase activity? Justify your answer briefly (3 pts).

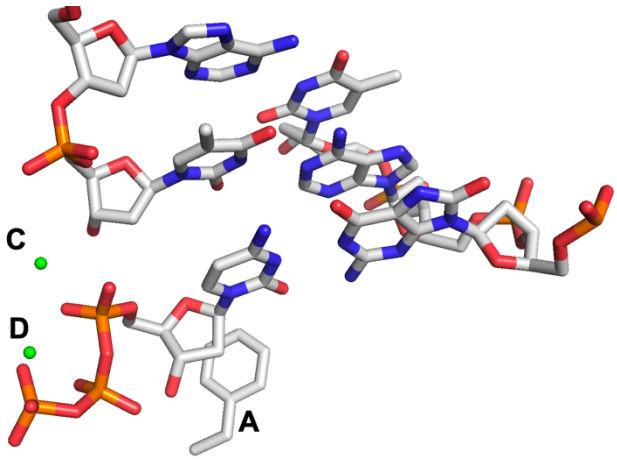
2.4: The drug is a nucleic acid molecule that contains an exact copy of human telomeric repeats. Scientists discover the drug is acting via Watson-Crick base pairing with something in the reaction.

What is the drug most likely binding to in the reaction? (2 pts)

Why does this binding of the drug influence the polymerase activity of telomerase? (2 pts)

Question 2 – 16pts. This figure shows the structure of the active site of an enzyme in complex with its nucleic acid substrates. Green spheres marked C and D are two divalent cations.

A – Label the 5' and 3' ends of the nucleic acids in the figure on the right. Label each of the bases in the figure on the right. Make sure you also identify any potentially modified or damaged bases. You can use abbreviations. 3pts



B – What is the general biochemical reaction catalyzed in this active site? – 2pts

C– Propose a function for amino acid A in the active site of the enzyme. Justify your answer based on the position of this amino acid relative to the other molecules found – 3pts.

D- Briefly indicate **ONE (and only one)** role for the divalent cation marked C in the mechanism catalyzed by the enzyme. 2pts.

E – Explain how the interaction observed between two of the nucleotides found in this structure is different from the interaction that you would have expected based on the materials studied in class. 2pts.

F – Based on the substrates present in the active site, propose a specific function or role for this enzyme in DNA metabolism. 4pts.