Week 7
Genetics: BIO-2306

The concepts this resource covers are the topics typically covered during this week of the semester. If you do not see the topics your particular section of class is learning this week, please take a look at other weekly resources listed on our website for additional topics throughout the semester.

We also invite you to look at the group tutoring chart on our website to see if this course has a group tutoring session offered this semester.

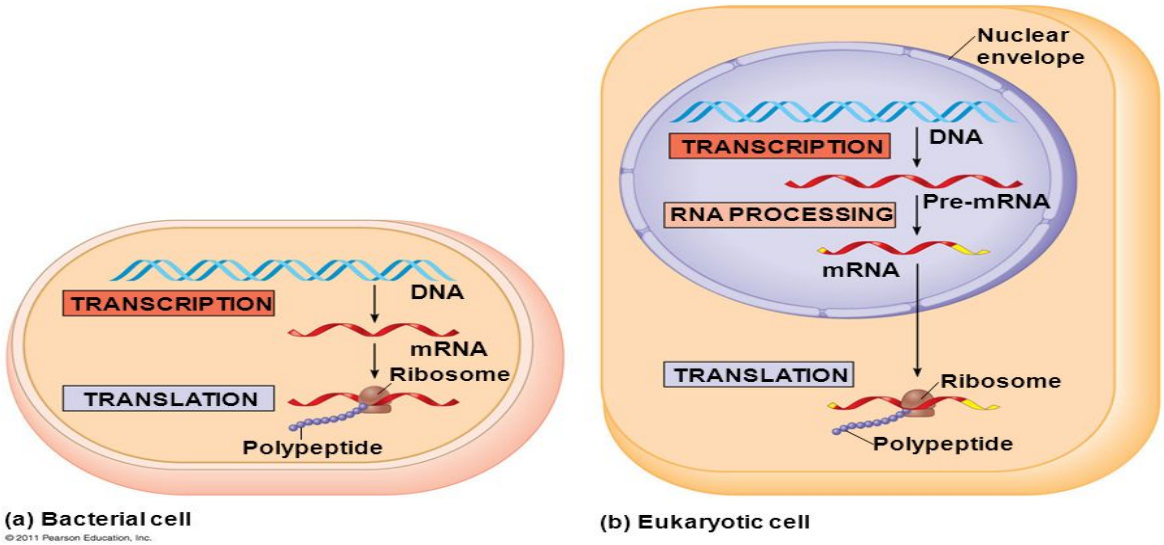
If you have any questions about these study guides, group tutoring sessions, private 30 minute tutoring appointments, the Baylor Tutoring YouTube channel or any tutoring services we offer, please visit our website www.baylor.edu/tutoring or call our drop in center during open business hours. M-Th 9am-8pm on class days 254-710-4135.

Keywords: Replication, semi-conservative, replication fork

Key Concept in Molecular Biology: The Central Dogma

DNA → RNA → Protein

Figure 17.3



The ***central dogma*** of molecular biology describes the flow from genetic information in a cell. **DNA** is the molecular storehouse of genetic code within a cell. DNA will replicate any time a cell passes through **S-phase** on its way to replication. Information encoded in DNA is *transcribed* to RNA which in turn is directly *translated* or assists with the translation of proteins.

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Note:** sometimes RNA will replicate, or will be *reverse-transcribed* (as may be seen with many viruses. Additionally, some *other types of RNA* may be transcribed or created that are ***not directly involved with translation*

Topic of the Week: ***DNA Replication Models*** (12.2-4)

Origin of Replication: the location where *DNA polymerase* and associated proteins bind to initiate DNA replication (**ori**)

Replicon: DNA that replicates from a ***single*** origin of replication

Prokaryotic Models: models of DNA replication seen on **circular** DNA

Theta Replication: DNA unwinds at a single origin of replication; replication forks on either side form with the single-stranded templates from each parent strand; replication will radiate out from either fork until two ***semi-conservative*** daughters are formed

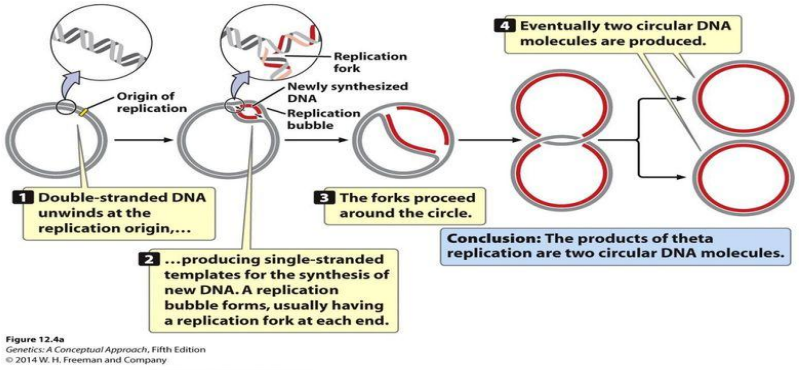

Figure 12.4a
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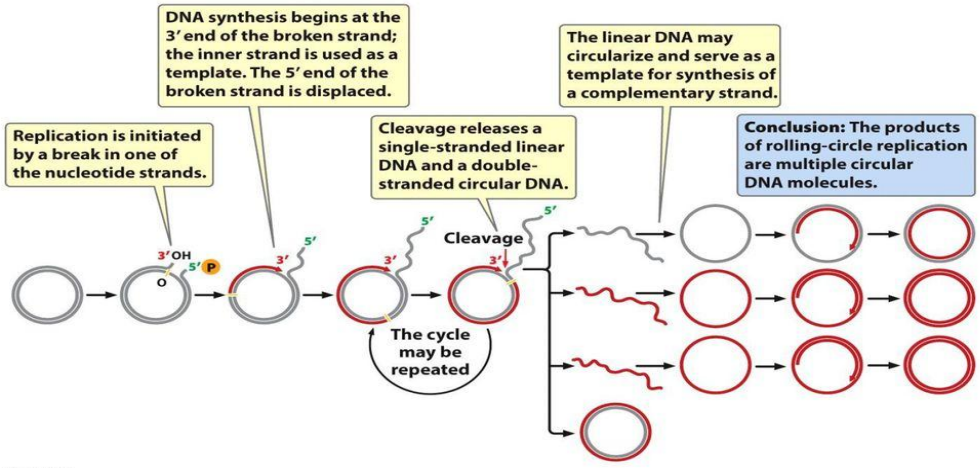
Rolling Circle Replication: A single stranded break leaves a free 3'-OH group on one end of the cut and a 5'-Phosphate (**P**) on the other end; dNTPs are added to the 3' end and the original strand unrolls like a spool of yarn; The original broken strand may be freed and serve as another DNA template



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Eukaryotic (Linear) Model: models of DNA replication seen on **linear** chromosomes
DNA replicates from many origins of replication; Replication forks expand out linearly until two meet each other, giving long stretches of new DNA.

Requirements for Replication:

Template: a template of single-stranded DNA (ie DNA must be unwound & separated)
Raw Materials: dNTPs are needed to be added to the free 3'-OH of the growing chain
Enzymes: needed to read, assemble, alter and join the DNA strands which are formed

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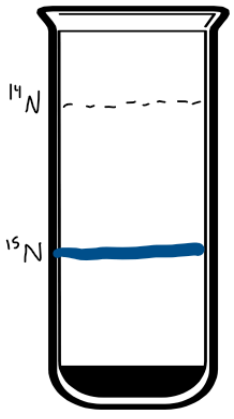
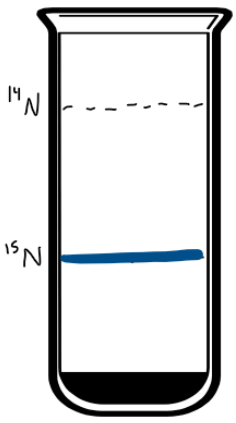
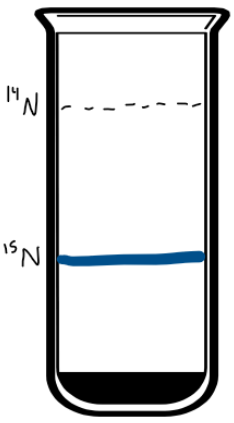
Highlight #1: The Meselson Stahl Experiment (12.1)

Theoretical Patterns of DNA Replication:

Conservative Replication: The original copy of DNA is copied each time and is completely conserved; new strands are copies and contain ***none*** of the 'parental' strand
Dispersive Replication: The original copy of DNA is
Semiconservative Replication: The original copy of DNA is split into two halves by breaking H-bonds, separating the strands. Each DNA strand acts as a *template* for DNA replication. Thus, each daughter has one *newly synthesized* and one parent strand.

Meselson and Stahl: a pair of scientists that showed that DNA replicated *semiconservatively*
Cells were raised in "heavy" ^{15}N medium. Some cells were spun in a centrifuge and some wereThese cells were removed and placed into a new container with ^{14}N medium. After a single replication, they were spun in a centrifuge.

Conservative	Dispersive	***Semi-Conservative
		

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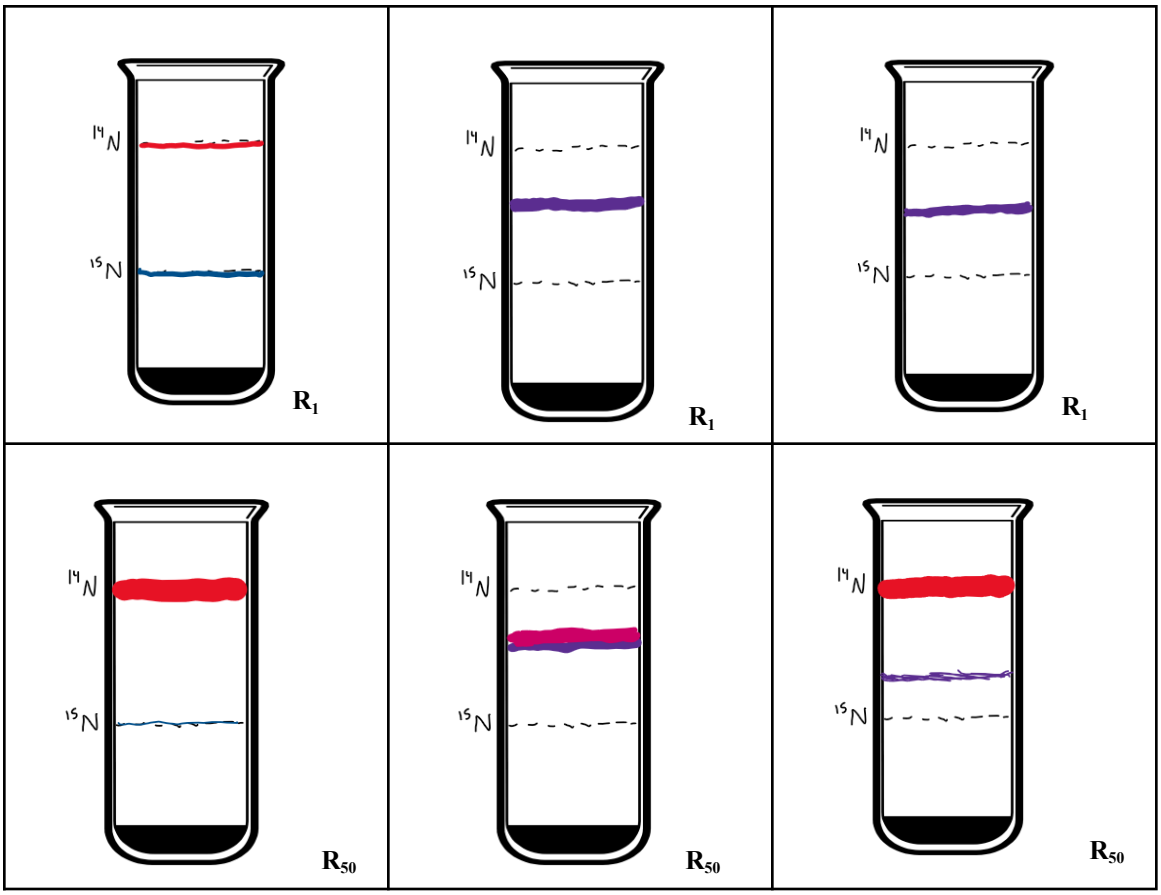


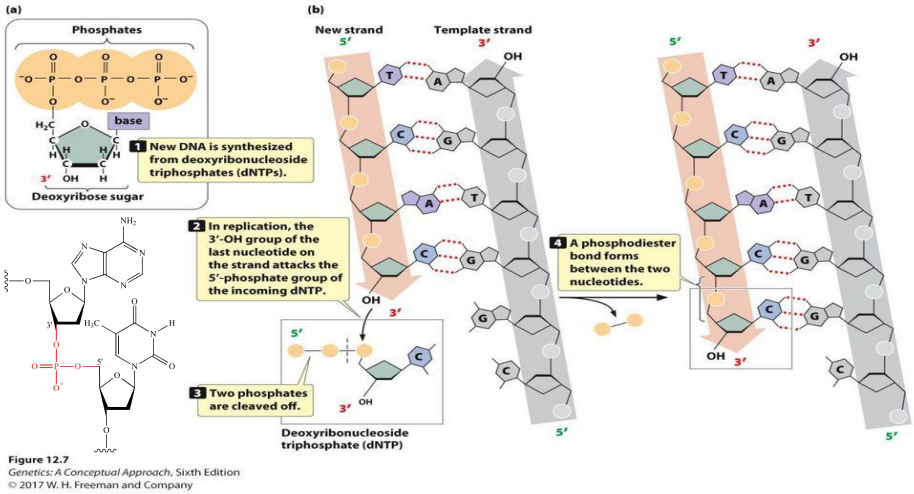
Above: these are the expected outcomes of the possible 'pellets' formed by the centrifugation of the DNA samples. As noted with three stars (***), semiconservative was the ***only*** form that Meselson and Stahl observed when they completed their experiment. Thus, they concluded that DNA replication **must be semiconservative**.

Highlight #2: **The Replication Bubble** (12.3)

Direction of Replication:

DNA polymerase adds dNTPs to the new strand (complementary to the template). dNTPs are added in the 5'→3' direction (ie we add to the **3'-OH**)

The linkage from the *dehydration synthesis* of the 5' phosphate and the 3'-OH is a **phosphodiester bond** (right)



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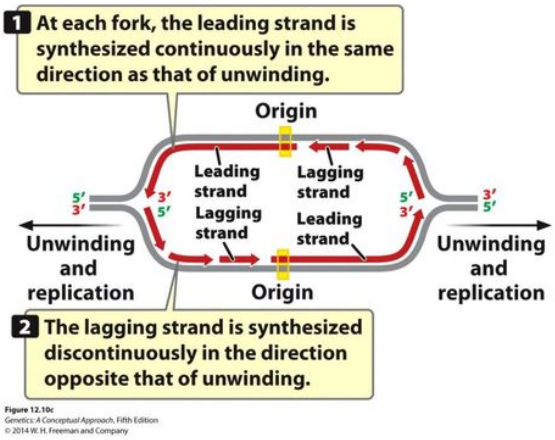
Continuous: the section of the template exposed from the fork in the 3' → 5' direction which can be continually synthesized (**leading strand**)
Discontinuous: the section of the template exposed in the 5' → 3' direction. *DNA-pol* must 'jump' backwards and replicate small fragments and then repeat this process (**lagging strand**)
Note: the leading and lagging strands *switch* at the origin of replication
RNA Primer: *DNA-pol* needs existing DNA to bind dNTPs to. RNA primers allow replication to start by using special *RNA-polymerases* to create short strands complementary to the template strand. These primers are converted to DNA and DNA polymerases begin synthesis (ie. Thus, a newly synthesized strand *must* begin with a *primer*)



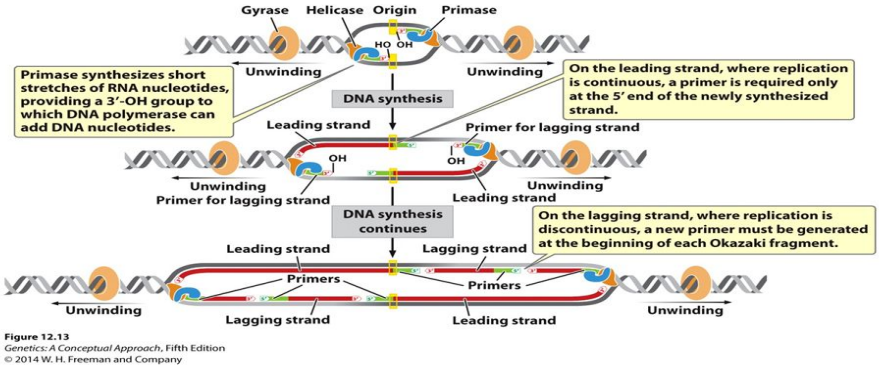
Comparison of Eukaryotic and Prokaryotic Replication:

Prokaryotes:

Initiation: initiator proteins bind to (**ori**) and begins unwinding (helicase binds)
Unwinding: ***helicase*** 'unzips' DNA helix by disrupting H-bonds between bases moving in the **5'→3'** direction on the lagging strand.
Single strand binding proteins (**SSB**s) bind DNA and prevent re-annealing.
DNA Gyrase cuts, untwists and reloins DNA downstream from either replication fork to decrease torsional strain of supercoiling.
Elongation: one single primer is needed on the leading strand; each **5' end** of an **Okazaki fragment** needs a primer

Okazaki Fragments: segments of discontinuous DNA synthesized on the lagging strand; ***DNA ligase*** joins the disjointed *Okazaki fragments* into a continuous stretch of new DNA.

DNA primase binds to helicase and forms RNA primers; ***DNA-pol I*** replaces RNA with DNA nucleotides; ***DNA-pol III*** catalyzes the addition of dNTPs to the growing strands of new DNA
Termination: termination occurs when 2 ends of replication bubbles meet.



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Eukaryotes:

Initiation: eukaryotic initiation requires "licencing" -or protein recognition- of each **ori**, then 2 Licensing Factors and protein ***ORC*** join to form active helicases

Unwinding: ***helicase*** 'unzips' DNA helix by disrupting H-bonds between bases

Elongation: one single primer is needed on the leading strand; each **5' end** of an **Okazaki fragment** needs a primer. Eukaryotic cells have many types of ***DNA-pol***; here are the important types:

DNA-pol α: has primase activity; creates RNA primer followed by a short stretch of DNA

DNA-pol δ: completes replication of the lagging strand

DNA-pol ε: replicates the leading strand

***DNA ligase*:** joins the disjointed *Okazaki fragments* into a continuous stretch of new DNA.

Termination: termination occurs when 2 replication bubbles meet

Telomeres: the ends of linear DNA in highly proliferating cells are replicated by an enzyme called ***telomerase*** (see the linked video for more info!)
https://www.youtube.com/watch?v=2NS0jBPurWQ

Highlight #3: Overview of Transcription (13.2)

Transcription: the synthesis of RNA from a DNA template using an *RNA-polymerase*

FYI: transcription will use a *DNA-Dependent RNA-Polymerase*. However, RNA replication would have an *RNA-dependent RNA-polymerase*, meaning it relies on an RNA template to synthesize RNA.

Structure: RNA is transcribed complementary and antiparallel to DNA; RNA synthesis occurs in the **5' → 3' direction**.

Template Strand: only one of the two strands of DNA will be transcribed, meaning it is bound by *RNA-pol* and will be complementary to (coding/antisense strand)

Nontemplate strand: the DNA strand *not* copied by *RNA-pol* which bears the **same sequence** as the transcribed RNA, but with T's instead of U's (non-coding/sense strand)

Substrates: the nucleotide monomers joined by the *RNA-pol*

Ribonucleoside triphosphate (rNTP)

Below: transcription unit, or the components of the section transcribed by ***RNA-pol***

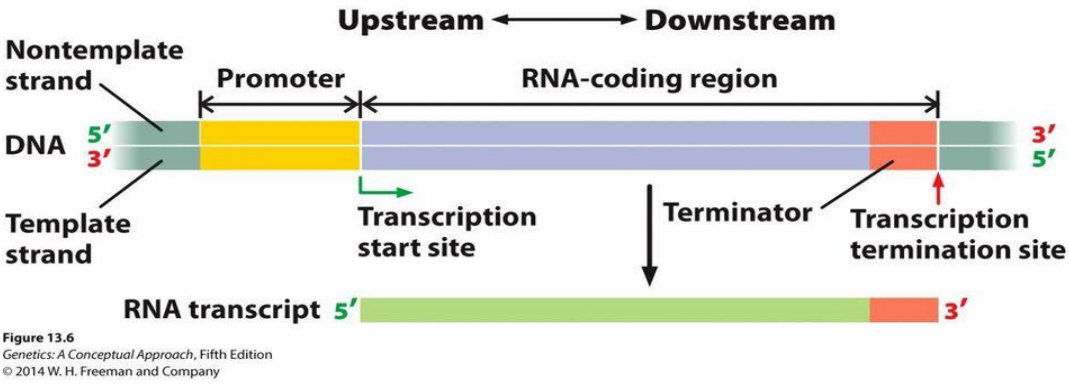

Figure 13.6
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Promoter: the region of DNA to which the transcription apparatus (***RNA-pol*** complex and associated proteins) binds

Transcription Start Site: location where the first nucleotide is transcribed

RNA Coding Region: the entire section of DNA transcribed by ***RNA-pol***

Terminator: the DNA sequence which causes ***DNA-pol*** to dissociate or causes cleavage of RNA transcript

Transcription Termination site: the spot where transcription is completed

Notations:

Upstream: away from terminator towards promoter

Downstream: away from promoter towards terminator

THINGS YOU MAY STRUGGLE WITH:

1. DNA replication will ***only*** happen in the 5' → 3' direction; that is to say, DNA replication only occurs when we add to the free 3'-OH. Thus, the 5' end will not change but the 3' end will **elongate**.
2. If a ***DNA-pol*** has a number, it is bacterial polymerase; if it has a greek letter, it is a eukaryotic.
3. When you consider the leading vs lagging strands, always remember that replication occurs in the **5' → 3'** direction; thus, the strand that is acting as the template must be in the 3' → 5' direction (proceeding into the replication fork) for replication to be continuous. If the template is 5' → 3' heading into the fork, replication on this strand will be *discontinuous*.

CHECK YOUR LEARNING

Concept Check: *(Answers found on last page)*

1. What type of DNA polymerase is less processive, but has 5'→3' exonuclease capabilities?
   a. *DNA-pol I*
   b. *RNA-pol II*
   c. *RNA-pol III*
   d. *DNA-pol III*
2. A mutation in a gene coding for ***DNA-pol δ*** causes an inactive form. What part of DNA replication would be most affected in a **Eukaryotic organism**?
   a. Leading strand primer formation
   b. **Ori** licencing
   c. Lagging strand polymerization
   d. It depends..
3. What does telomerase do? What type of cells might have telomerase? How might a mutation of telomerase affect clonal evolution (cancer development)? (**see the video!**)

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4. Which strand am I: the template runs 3'→5'
    a. What/which enzyme(s) is/are going to be more active on me? (Prokaryotic? Eukaryotic?)
5. A certain mutation to the promoter prevents everything _____ from it, meaning that the RNA transcript will not be formed
    a. Upstream
    b. Across the river
    c. Across
    d. Downstream

You Try: Click the link to apply your knowledge!
Practice Drawing (Replication Bubble)**:**
https://docs.google.com/drawings/d/1EOJxiH_Ftk7BTD5xXAh4apr5_4St9bgYBZEO75k-TR8/edit?usp=sharing

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Answers to check your learning questions are below!

Answers:

1. **A.** DNA-pol-1
2. **C.** Lagging strand polymerization
3. Telomerase extends the end of chromosomes
    a. Steps:
        i. G-rich 3' overhang is extended
        ii. C-rich 5' undehang is expanded using the RNA component of telomerase
        iii. RNA is turned into DNA
    b. Cells:
    c. Stem cells/marrow cells, germ cells, anything rapidly dividing such as cancer cells
    d. Clonal Evolution
        i. Telomerase increases the fitness of cancer cells, granting them essentially indefinite replication
4. Lagging strand
    a. DNA ligase
    b. [Prokaryotes] Helicase and primase form a complex on the lagging strand (primase is going to be very active though, bc it has to keep creating new okazaki fragments); a lot of DNA pol I activity as well
    c. [Eukaryotes] DNA-pol-δ
5. **D.** downstream

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