Next Step TEST PREP

# MCAT Super Review

## Genetics

March 31, 2018

# Welcome!

- If you haven't been to one of our webinars before, here's how it works. Each session is meant to be:
  - Interactive
  - Problem-focused
  - Specific to your needs (so ask questions!)
- This is not just a lecture! You can benefit most by:
  - Raising your hand and speaking
  - Asking questions in the chat box

- ✓ Is your microphone on and available?
- ✓ Can you find the hand-raise button?
- ✓ Can you find the Chat or Questions box?
- ✓ Let me know if you have technical issues!

# Who Is Next Step?

- Began in 2009 as a tutoring company
- Focus on graduate admissions tests only
- Team of educational experts
- First company to have materials built from ground up for 2015 MCAT format
- Now the first company to have new 2018 MCAT Interface

✓ We never stop improving our materials!

# Who Am I?

- Clara Gillan
  - Course Content Director at Next Step
  - Senior instructor; 526 MCAT score
- Managed development of Next Step's updated interface
- Written and edited thousands of questions

# Biology Content Review

Congrats on making progress through our MCAT course! Today let's focus on bio:

- **Overall study strategies**

  *Active learning*

  *Big-picture perspective*

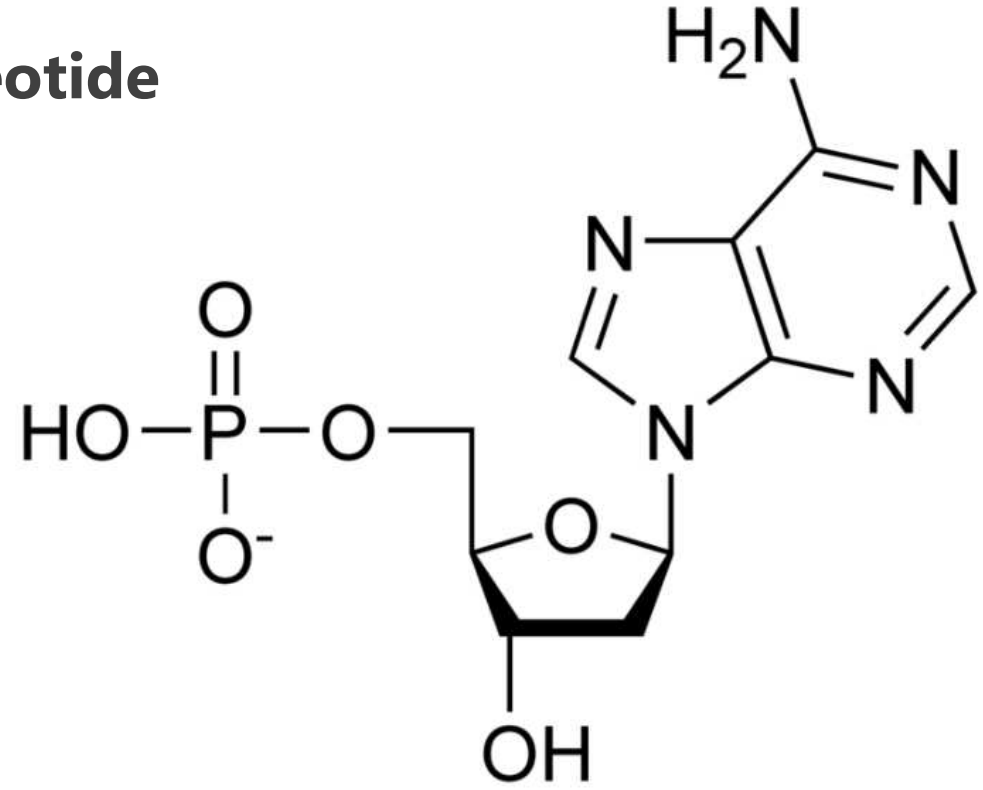
  *Test-like thinking*

**When studying, ask yourself …**

- *Why does this matter for future physicians?*
  - *Cell biology: How do structures contribute to the function of an organism?*
  - *Genetics: How does a topic contribute to real-world issues? What consequences would dysfunction of a given system have?*
  - *Physiology: How do all the pieces fit together? How does a system respond to changes in the environment? What would dysregulation cause? How does a system contribute to our ability to function?*

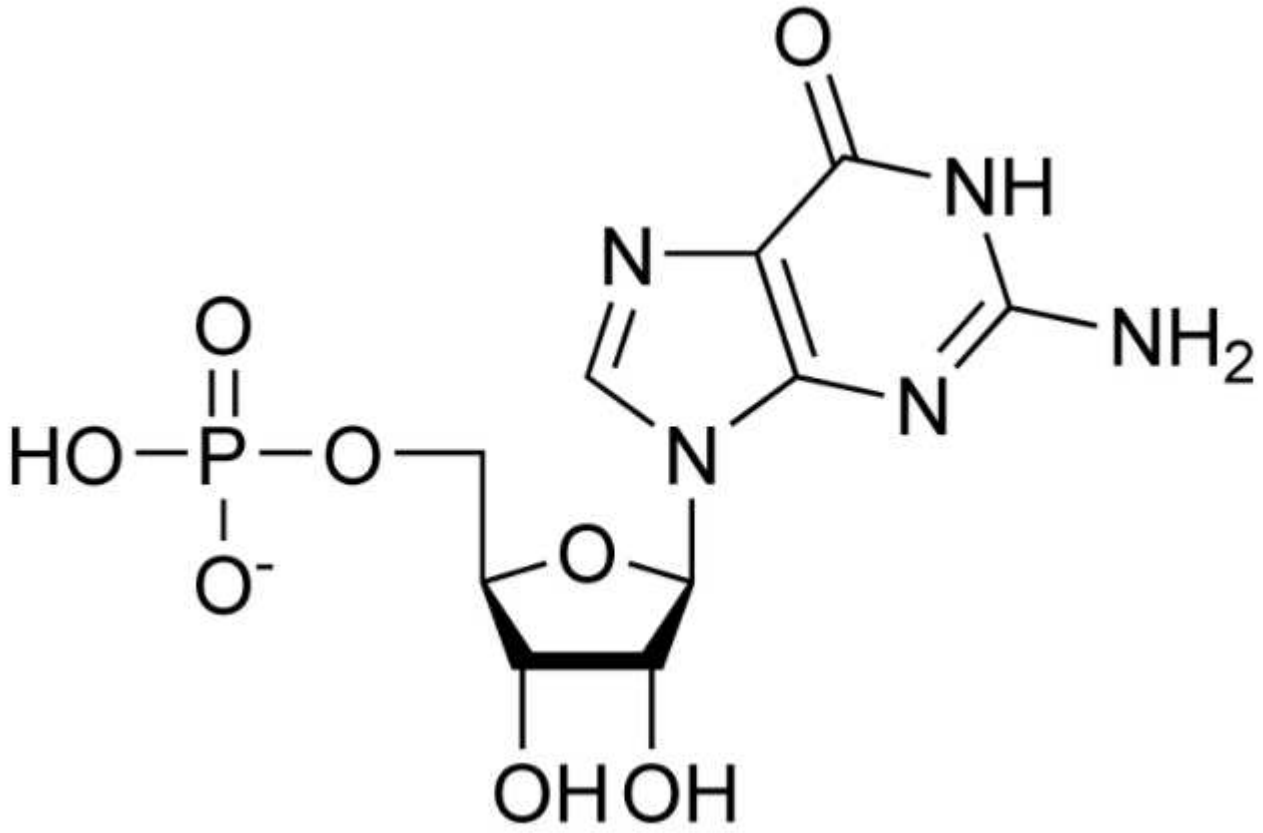
# DNA and RNA

- DNA = deoxyribonucleic acid
- Monomer = nucleotide



# DNA and RNA

- **RNA = ribonucleic acid**



# DNA vs. RNA

- DNA
  - Contains A, G, T, C
  - Typically double-stranded
  - Found in nucleus; storage molecule
  - Sugar = deoxyribose
- RNA
  - Contains A, G, U, C
  - Typically single-stranded
  - Found in nucleus and cytoplasm; short-lived
  - Sugar = ribose
  - Can catalyze reactions (ribozymes)

# MCAT Question: DNA and RNA

12. The most memorable difference between DNA and RNA relates to their composition. While thymine is a building block in DNA, it is replaced by uracil in RNA. Which of the following is another functional difference between DNA and RNA?

A) The genome of viruses is exclusively made up of DNA.

B) The inherent instability of RNA molecules renders them unable to store genetic information.

C) Certain RNA molecules possess the ability to catalyze biochemical reactions, while DNA molecules cannot.

D) RNA molecules, unlike DNA, are incapable of hydrogen bonding.

# MCAT Question: DNA and RNA

1. What is a major difference between the human genome and that of *E. coli*?

A) The human genome contains $10^6$ base pairs, while that of *E. coli* contains $10^9$.

B) The genome of *E. coli* contains many more extraneous segments of DNA than the human genome.

C) The *E. coli* genome is contained within a few chromosomes, while the human genome is composed of 46.

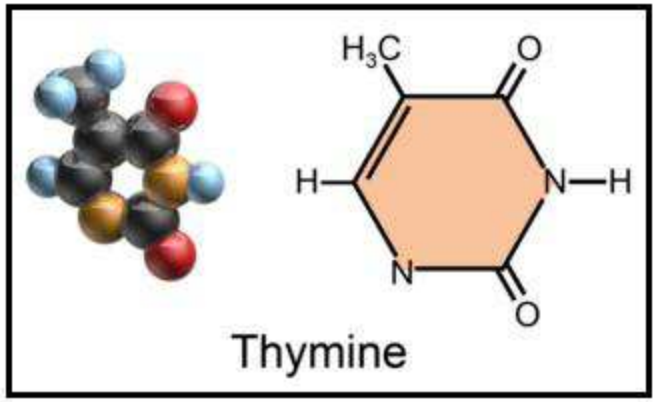
D) The human genome includes multiple chromosomes, while that of *E. coli* is composed of a single circular chromosome.

# Transcription: An Overview

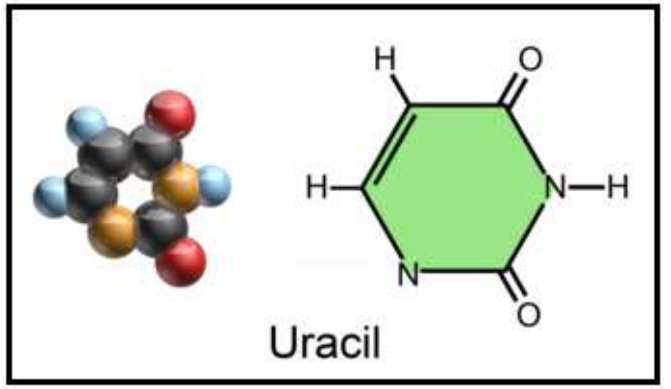
- **DNA → mRNA**

***double-stranded***
***A, C, G, T***
***stored in nucleus***

***single-stranded***
***A, C, G, U***
***rapidly degrades***

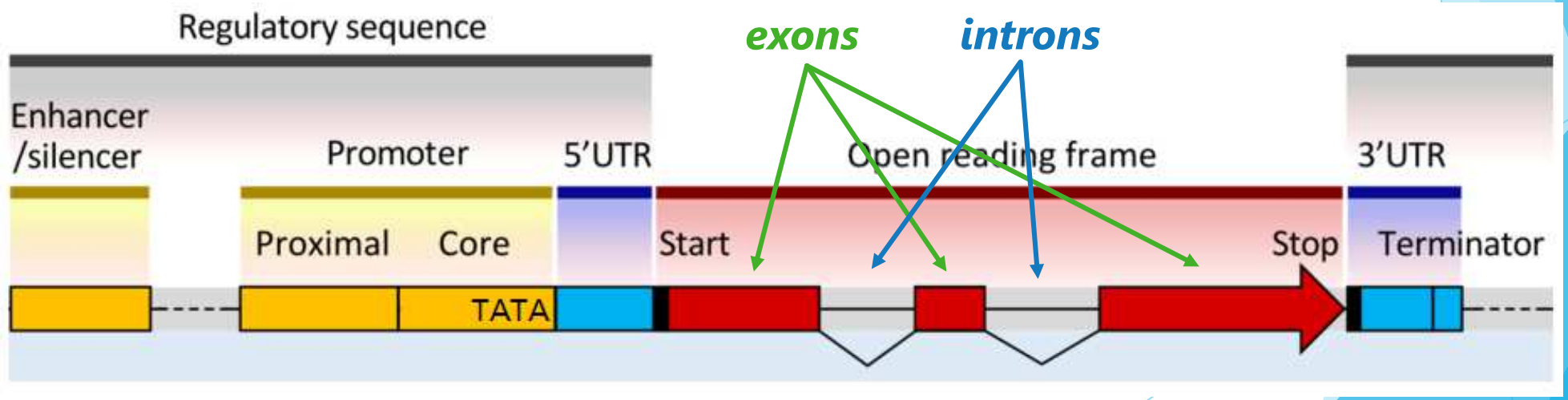



- **Initiation**
  - **RNA polymerase II binds promoter**
  - **DNA is unwound**
  - **Role of transcription factors?**



# Transcription: An Overview

- **Elongation**
  - **RNA polymerase travels 3′ → 5′** ***(adds nucleotides 5′ → 3′)***
  - **DNA re-winds after RNA pol passes**
- **Termination**
  - **RNA pol reaches termination site, detaches**



# Transcription: A Common Point of Confusion

- Only one strand is transcribed *(not both!)*
- Antisense strand → *is transcribed*
  - AKA template strand, noncoding strand
  - Complementary to product mRNA
- Sense strand → *is NOT transcribed*
  - AKA coding strand, nontemplate strand
  - Identical to product mRNA *(except U vs T)*

*5′-ATGCCGA-3′*

↓ *transcription*

*3′-UACGGCU-5′*

↓ *reverse transcription*

*5′-ATGCCGA-3′*

- A segment of mRNA is transcribed from a dsDNA molecule in which the antisense strand is 5′-ATGCCGA-3′. The mRNA strand is then reverse transcribed. What will be the sequence of the cDNA immediately produced?

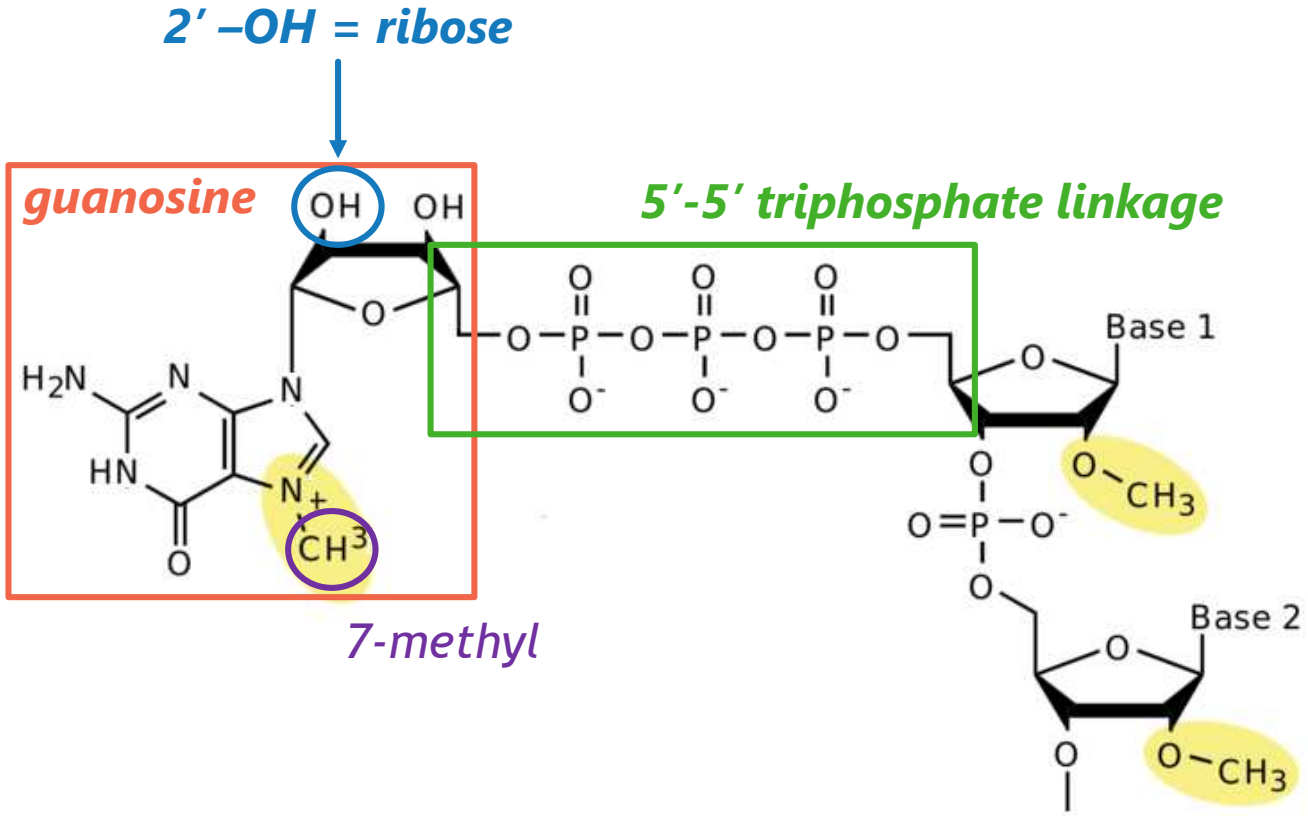
*"complementary" DNA*

# Post-Transcriptional Modifications

- **Location of transcription:** *nucleus*
- **Location of translation:** *ribosomes in cytosol / bound to rough ER*
- **But where do the modifications take place?**
- **Three main events**
  1. **Addition of a 5′ methylguanosine cap**
  2. **Addition of a 3′ poly-A tail**
  3. **Splicing of introns and ligation of exons**
- **"Pre-mRNA" =** ***hnRNA***
  ***heteronuclear***

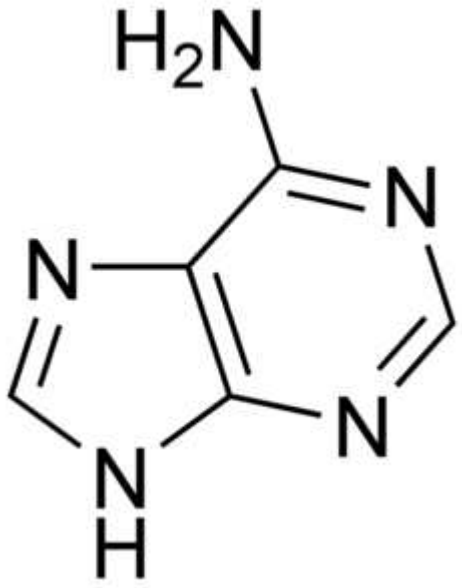
# 5’ Capping

- First: how can the 5’ end be distinguished?
  - “5’ free phosphate”
- Capping begins before transcription ends
- Protects from enzymatic degradation in cytosol




# 3’ Polyadenylation

- How can the 3’ end be distinguished? *“3’ free -OH”*
- Polyadenylation = *addition of >200 adenine residues*
- Enzyme-catalyzed
  - DNA polymerase? *no!*
  - “Polynucleotide adenyltransferase”
- Two main functions
  - Binding site for nuclear export protein
  - Protects from degradation at 3’ end
- Longer tail = more time before degradation



# Last But Not Least: Splicing

- Exons = coding
- Introns = noncoding
  - Present in pre-mRNA
  - Not present in mature mRNA
- Do prokaryotic genomes include introns?

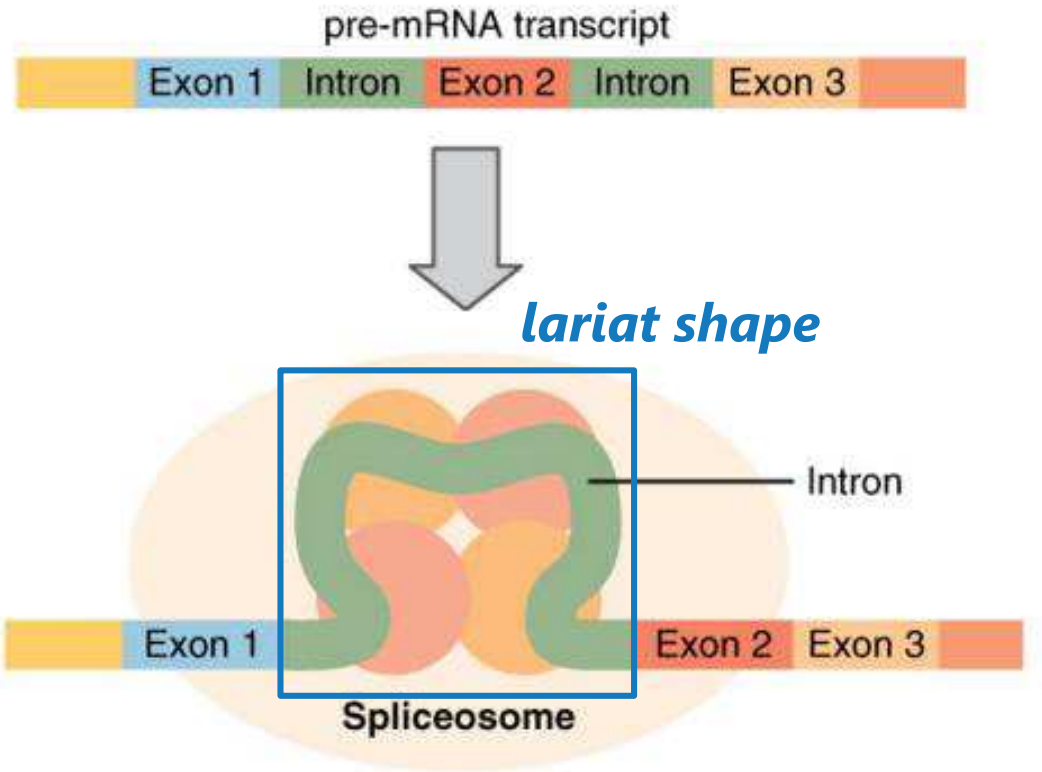
# Splicing Mechanism

- Spliceosome
  - Large RNA-protein complex
  - Assembles on hnRNA transcript
  - Recognizes intron-specific sequences
- snRNAs = *small nuclear RNAs*
- snRNA + protein = snRNP

⇩

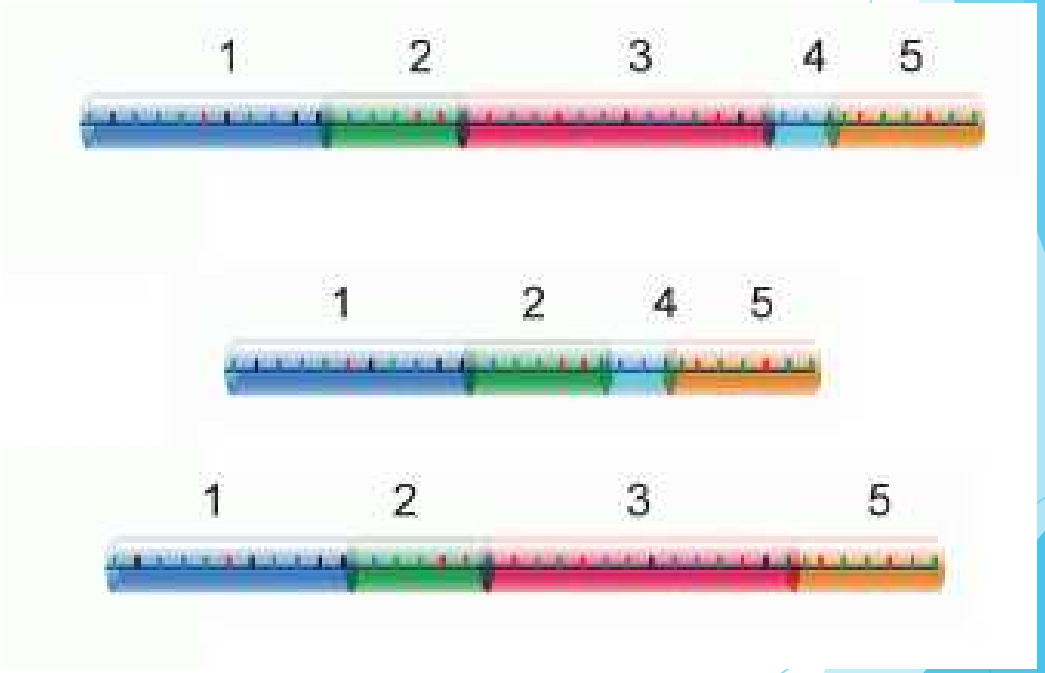
*small nuclear ribonucleoprotein*

- Afterward, exons ligated



# Alternative Splicing

- # of human genes (estimated): ≈ *20,000*
- # of human proteins (estimated): > *200,000*
- How is this possible?
  - Alternative splicing
  - Introns are still spliced out…
  - …BUT so are some exons!
  - Remaining exons are ligated
- One gene → up to 1,000 proteins!



# MCAT Question: Post-Transcriptional Modifications

4. The human genome contains a large number of repetitive sequences that have no known function. What happens to these sequences during the life of a cell?

A) These sequences are removed during meiosis to prevent their inheritance by the next generation.

B) These sequences are translated, but the proteins that they code for are immediately destroyed.

C) These sequences are spliced out before transcription takes place.

D) The sequences are spliced out before translation takes place.

# MCAT Question: Post-Transcriptional Modifications

11. A spliceosome is a complex structure assembled from snRNAs and their associated proteins. If an organism was suddenly unable to produce spliceosomes, what would be the likely result?

A) Transcription of mRNA from DNA would no longer occur.

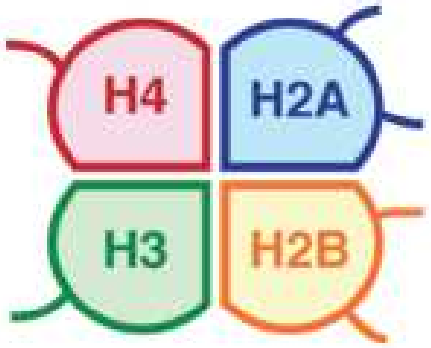
B) The dysfunctional machinery would severely limit DNA replication.

C) The organism would produce mRNA identical to pre-mRNA.

D) The recombination of different exons would not occur, limiting the diversity of gene products.

# DNA Packaging

- "Histones" → *proteins around which dsDNA winds*
  - Help form a compact structure
  - Core octamer complex
- "Nucleosome" → *histone complex + wound DNA*
  - "Beads on a string"
- 5 distinct histone proteins in human cells
  - Core: H2A, H2B, H3, H4
  - Linker: H1

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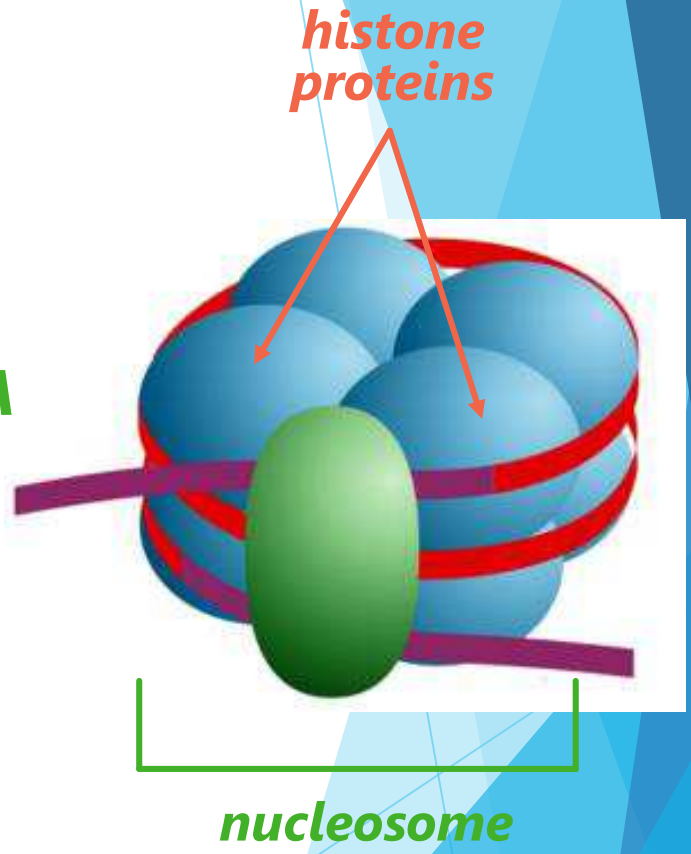
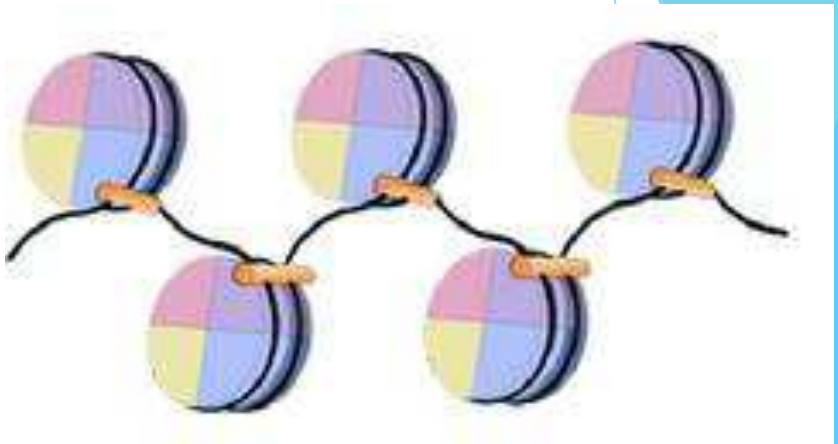


# Forms of Chromatin

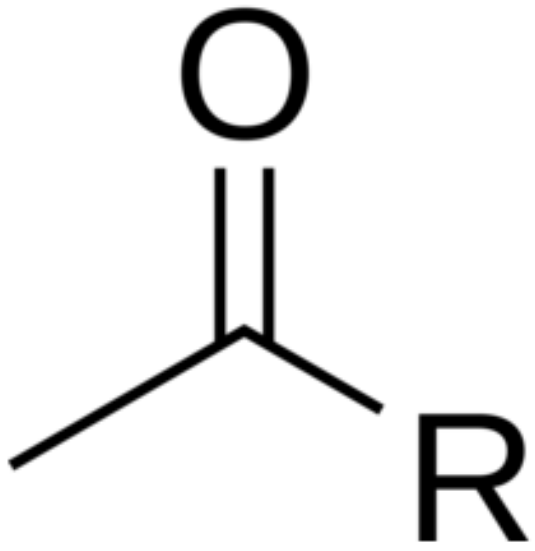
- **Euchromatin**
  - Loose structure
  - Appears light under a light microscope
  - Promotes transcriptional activity
  - When would this form dominate?
    - *S phase (DNA replication)*



- **Heterochromatin**
  - Compact structure, appears dark under light microscope
  - Represses transcriptional activity
  - When would this form dominate?
    - *mitosis (chromosomes condense)*

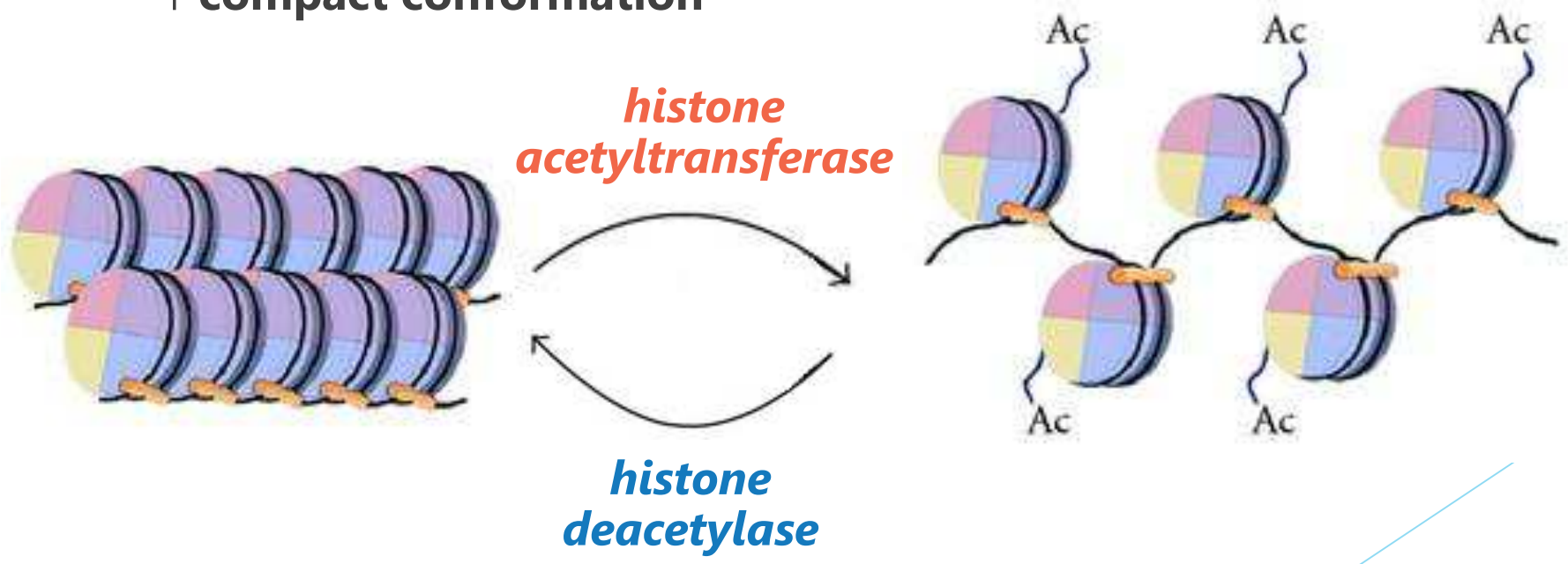
# Histone Modifications

- As proteins, histones can undergo *post-translational* modification
- Acetylation, deacetylation, phosphorylation…
- Histones = *alkaline (basic)* = *positive (+)*
  - Phosphates on DNA = negative
- Acetylation
  - Catalyzed by histone acetyltransferase
  - Removes (+) charge
  - *Decreases* histone-DNA attraction
  - ↑ loose conformation



# Histone Modifications

- **Deacetylation**
  - **Catalyzed by histone deacetylase**
  - **Increases (+) charges present**
  - **_Increases_ histone-DNA attraction**
  - **↑ compact conformation**



# MCAT Question: DNA Packaging

2. The correct sequence of DNA packaging in chromosomes, from the smallest component to the most complete form, is:

A) double-stranded DNA → chromatin → histones → nucleosomes.

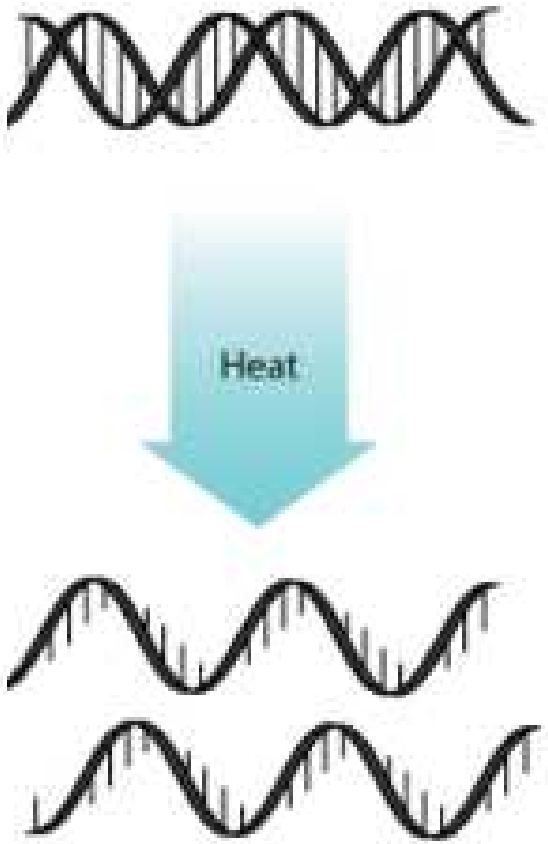
B) double-stranded DNA → histones → nucleosomes → chromatin.

C) chromatin → double-stranded DNA → histones → nucleosomes.

D) chromatin → double-stranded DNA → nucleosomes → histones.

# PCR – Why Do We Use It?

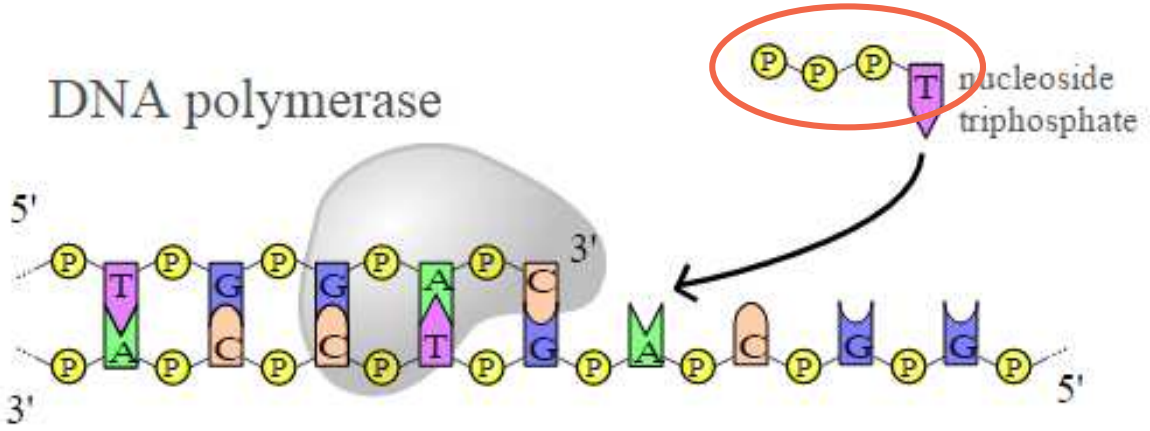
- PCR = *polymerase chain reaction*
  - Amplification of a sequence of interest
  - Like DNA replication in the lab!
- First, some terms to understand:
  - Hybridization
  - Denaturation *("melting")*
  - Annealing



# PCR "Ingredients"

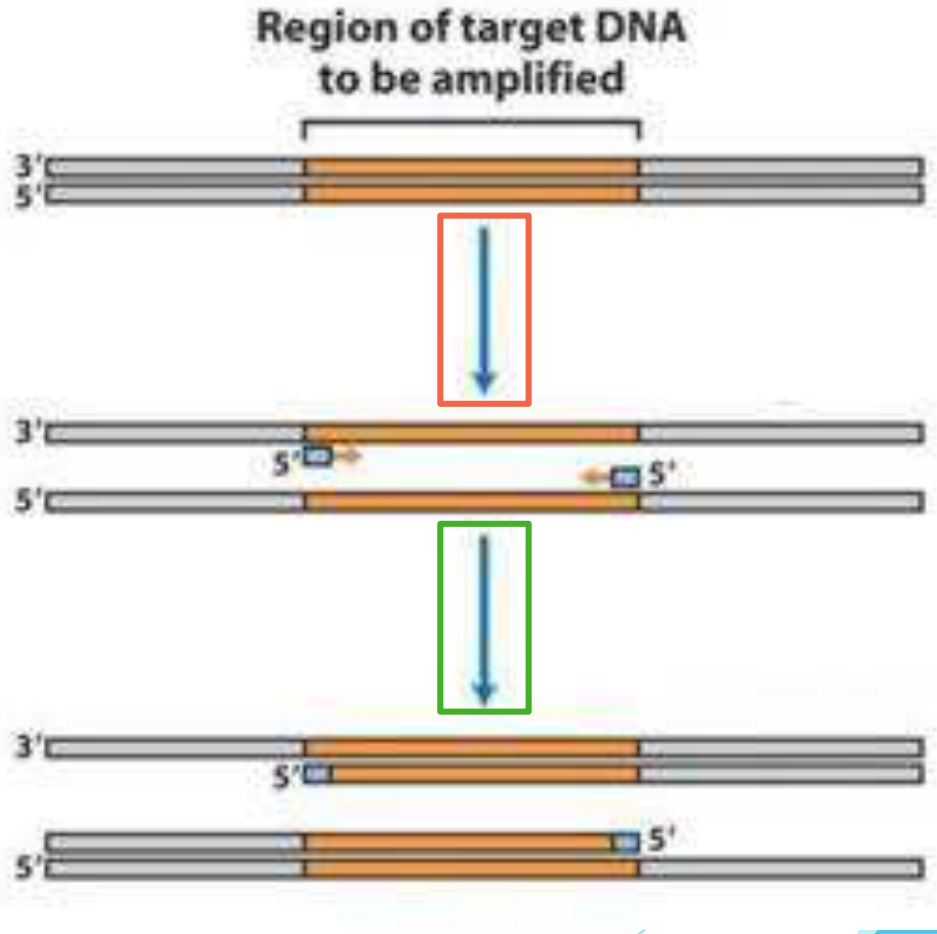
*Thermus aquaticus*

- *Taq* polymerase
  - Why not a eukaryotic polymerase?
- DNA oligonucleotides = *primers*
- DNA sample of interest
- dNTPs = *deoxynucleotide triphosphates*
- Proper buffer



# PCR Method: Repetitive Cycles

1. Denaturation (95° C)
   - *this breaks the dsDNA!*
2. Annealing (50-65° C)
   - *why such a wide range?*
3. Extension (72°)
4. Repeat!



# Restriction Enzymes

- Also known as restriction endonucleases
- Used to make recombinant DNA
- Leave "sticky ends"
  - Why?
- Rejoined by *DNA ligase*

*cleaves phosphodiester bond*


EcoRI recognition sequence

# Example: Restriction Enzymes

- **Which of these likely serves as a recognition sequence for a restriction enzyme?**

CCCGGG
GGGCCC

ATGTA
TACAT

- **A geneticist wishes to ligate two fragments of bacterial DNA that are currently found in separate plasmids. He should first:**
  - **cut both plasmids with the same restriction enzyme.**
  - **cut both plasmids with different restriction enzymes.**
  - **either of the above; it doesn't matter.**

# DNA Libraries

*bacterial plasmid / virus that "holds" the fragment*

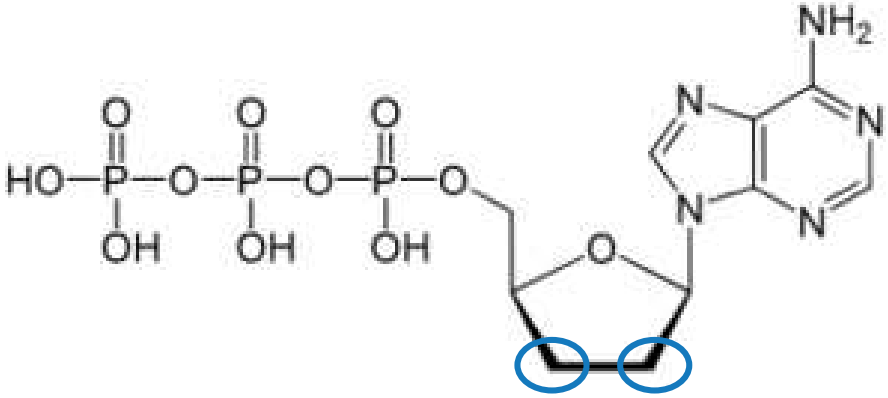
- Many DNA fragments stored in "vectors"
- Allows fragments to be kept for later use
- Genomic library → contains all DNA from an organism
  - Restriction digest → ligation into vector → transfection
- cDNA library → contains complementary DNA *(no introns!)*
  - mRNA obtained → reverse transcribed → made into dsDNA w/ DNA polymerase

# Sanger Sequencing

- Older technique (1977)
- 4 test tubes with these "ingredients":
  - ssDNA template (what we're sequencing)
  - A polymerase enzyme
  - A DNA primer
  - High [] of 4 dNTPs (dATP, dTTP, etc.)
  - Low [] of 4 labeled ddNTPs (ddATP, ddTTP, etc.)

*in all 4 tubes*

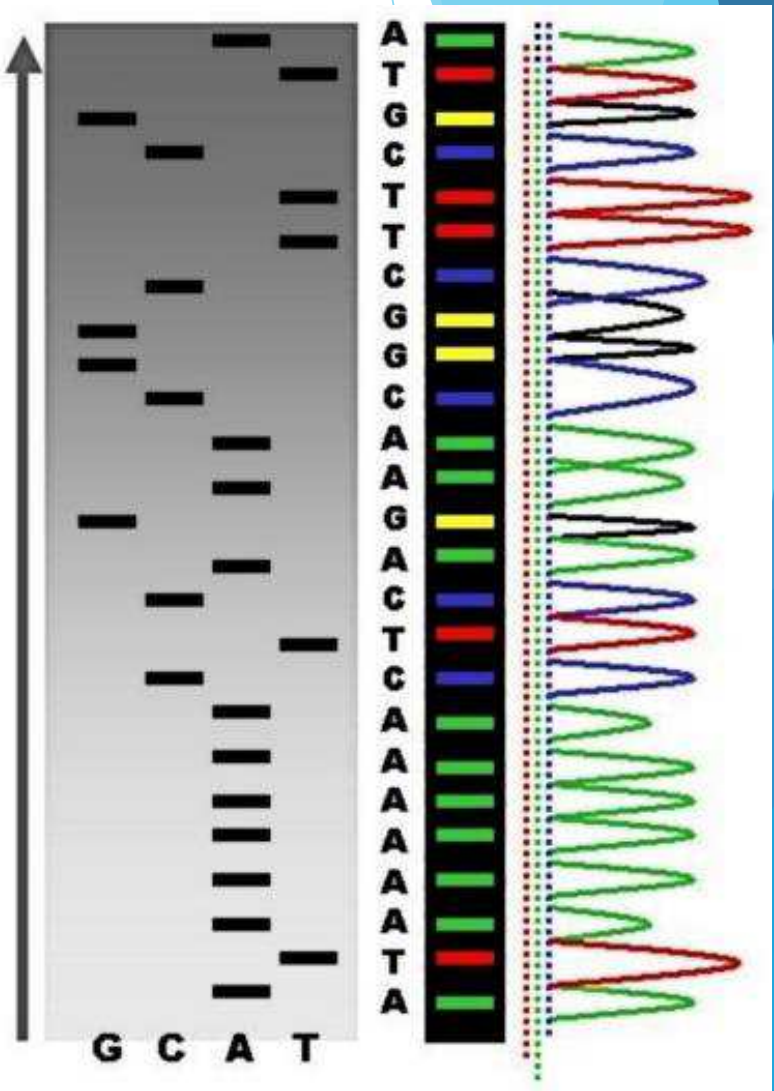
*one ddNTP in each tube*



*ddATP*

# Sanger Sequencing

- Replication occurs in each tube
- What happens when a ddNTP is incorporated?
  - *replication terminates*
  - *happens many times in each tube!*
- Why must [dNTPs] >>> [ddNTPs]?



# Next Step: Core Values

Educate Daily

Approachability

Authenticity

Professionalism

Ownership

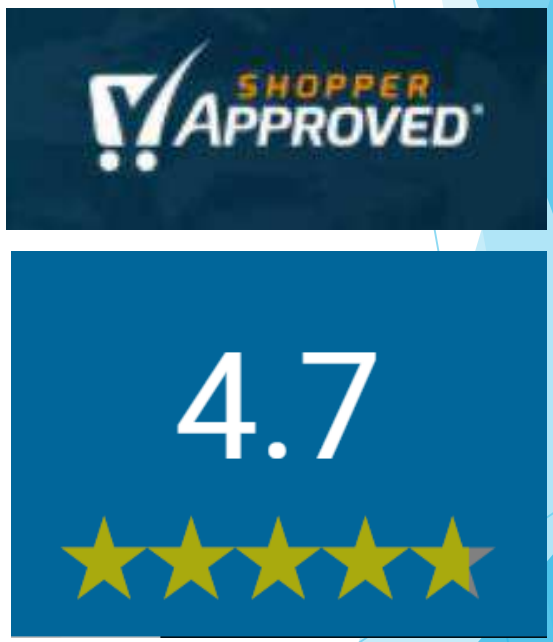
**We are dedicated to providing personalized support, advice and prep options that match each student's individual needs.**

STUDENTS HAVE A CHOICE IN TEST PREP

# Students Have a Choice

- ✓ **Over 50,000 students have used Next Step Test Prep in their MCAT Prep journey**

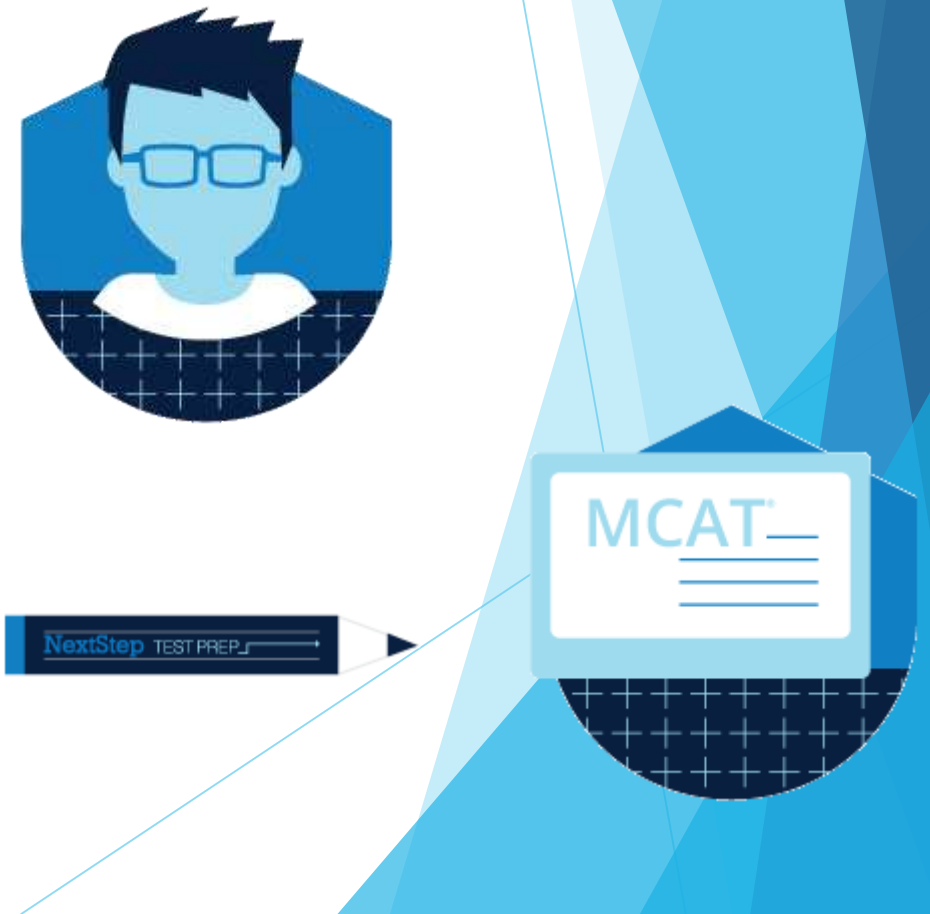
- **Always up-to-date content, strategy and tests**
- **Guaranteed Satisfaction**
- **Expert instructors on call for you**
- **No call center – instead, Academic Managers guide you all the way!**



# Personalized Options

✓ **No matter your study style, subject expertise, or MCAT goal, Next Step has an option for your personal needs and lifestyle.**

- **Self-Prep Materials and Planning**
- **Guided Online Study with Free Extra Help**
- **Flexibility and Personalization**
- **One-on-One Tutoring**



# Next Step: Educate Every Day

- ✓ **Use this high-value FREE practice to build a study plan suited to your goals, needs, and schedule.**

## Industry's Best Free MCAT Practice Bundle

- **Half-length MCAT diagnostic**
- **Full-length MCAT exam**
- **450+ Question Science Content Diag exam**
- **Test Review Videos**
- **Multiple QBank Samples**
- **16 Test & 4 Content Review Videos**
- **Proprietary Study Plan Generator**
- **Aligned to new MCAT 2018 Interface**

## Sign up for our FREE Practice Bundle:

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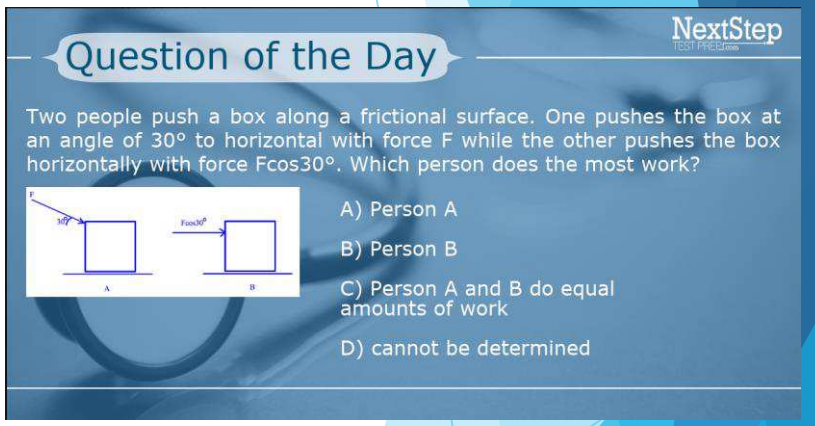
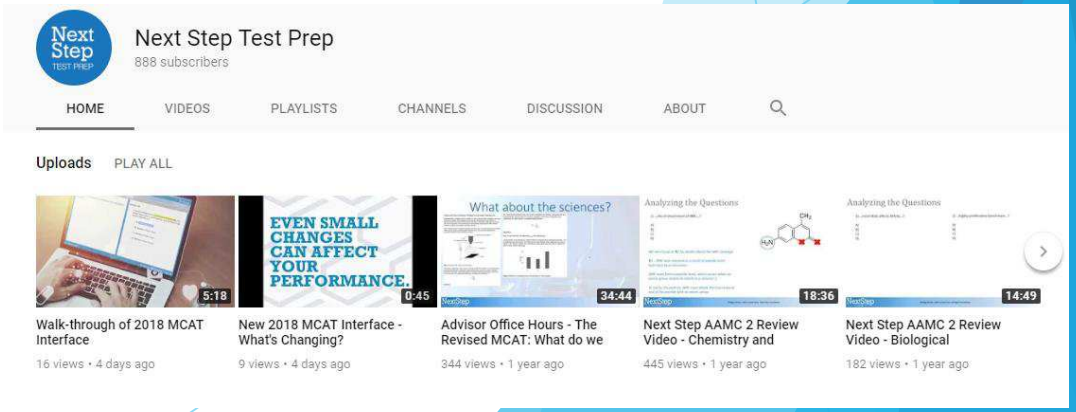
# Additional Free Resources

✓ **Supplement your prep with additional support tools**

- **Question of the Day Quick Prep**
- **YouTube, Facebook and Instagram Content**
- **Ongoing Public Webinars and Q&A Sessions**
- **MCAT Blog: Content and Admissions**
- **Next Step MCAT Forum**

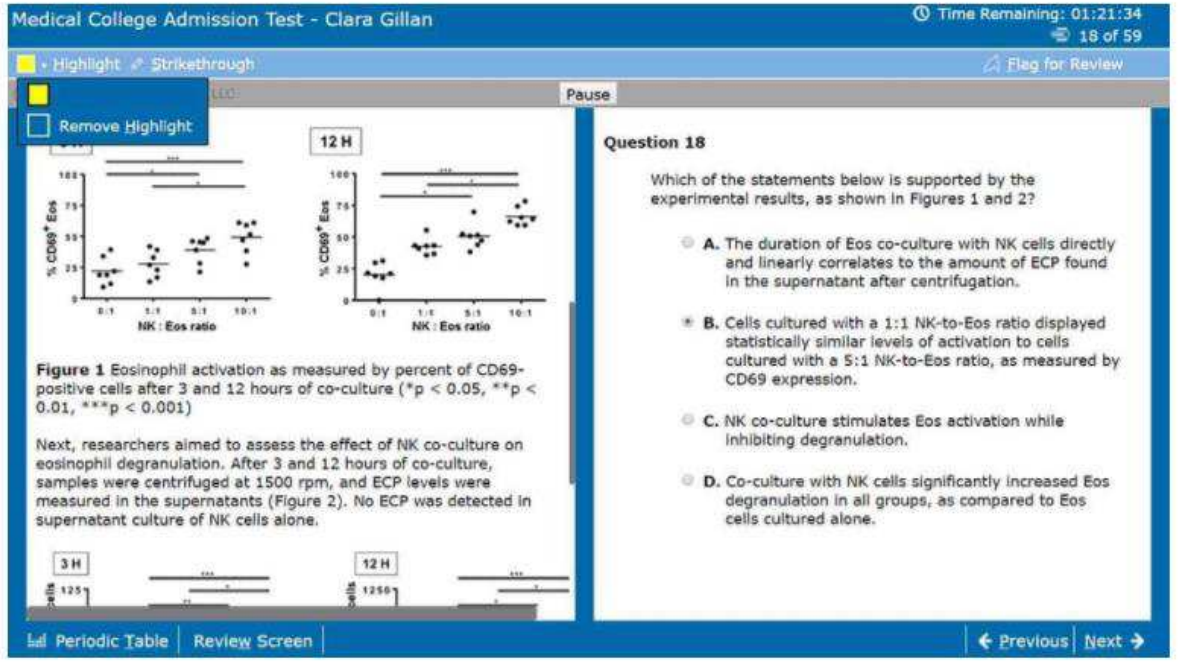


# New 2018 MCAT Interface

Next Step TEST PREP

- New Highlighting features
- New Strikethrough features
- New Keyboard Shortcuts
- New Navigation/Review Screens



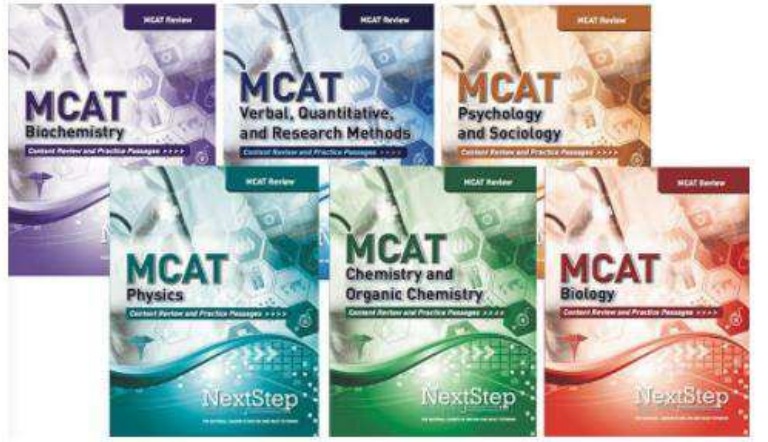

**Next Step is ready. Are you?**

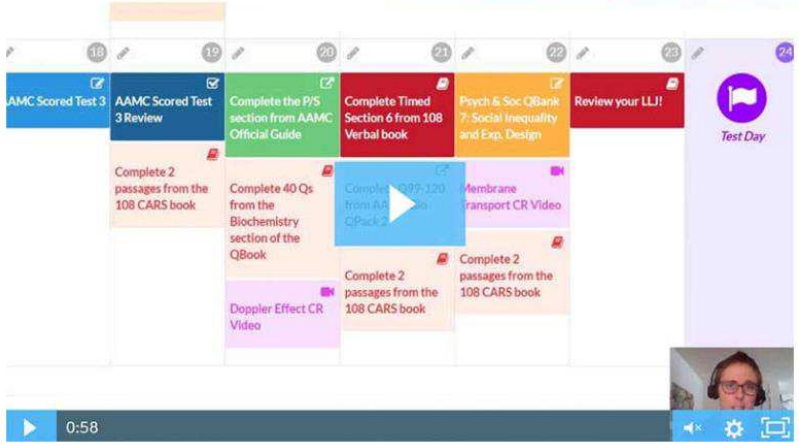
✓ **Your practice experience matters! Prep with the most realistic testing environment with Next Step.**

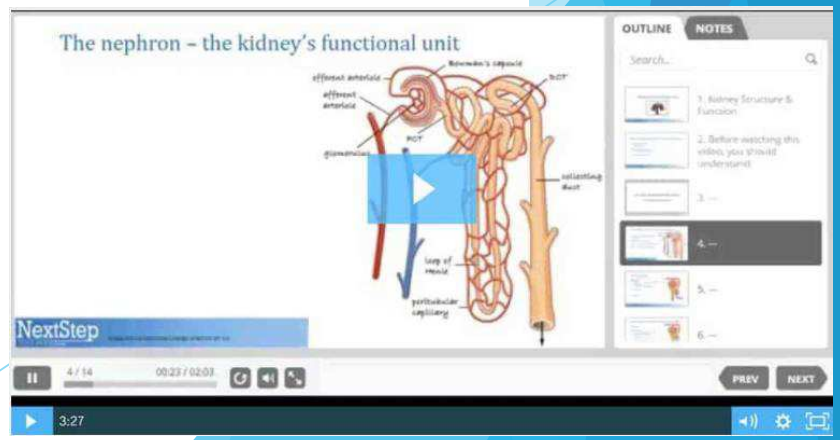
# Take the Best Next Step

✓ **Others say it. We deliver it.**

- **Most up-to-date Lesson Review Books in 4-color**
- **QBank with passage and discrete question types**
- **Exclusive Study Plan Generator personalized for you**
- **Hundreds of hours of videos**
- **Private, small-group Office Hours 5 days a week**
- **Direct access to MCAT Content Team**
- **Affordable prep options: from books to tutoring**



# MCAT Study Options

- **Best-in-Class MCAT Tutoring Packages**
  - Variety of packages: Crash Course to Elite
  - Choices include our MCAT Online Course
  - Personalized Study Plan for each student
  - Top-scoring tutors

- **Most up-to-date MCAT Course**
  - All new books in 4-color, all online AAMC resources
  - 10 full-length exams aligned to new interface
  - Live online office hours for any Q&A held 5 days per week
  - Study Plan Generator to match each student's strengths, weaknesses and schedule needs

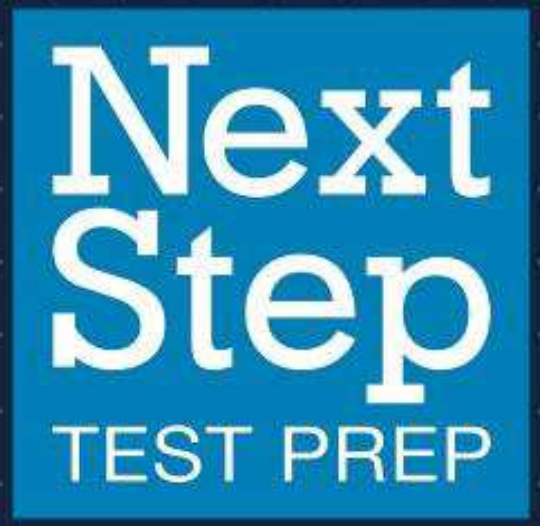
- **MCAT Practice Test Bundles**
  - Available in 4-, 6-, and 10-pack bundles
  - All aligned to new 2018 interface

Next Step
TEST PREP

# Get Solid Advice for Your Next Step

## Schedule a one-on-one consultation with an Academic Manager.

**REQUEST IN TODAY'S WEBINAR SURVEY.**




# Questions?