EPIGENETICS PART 1

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CASE STUDY

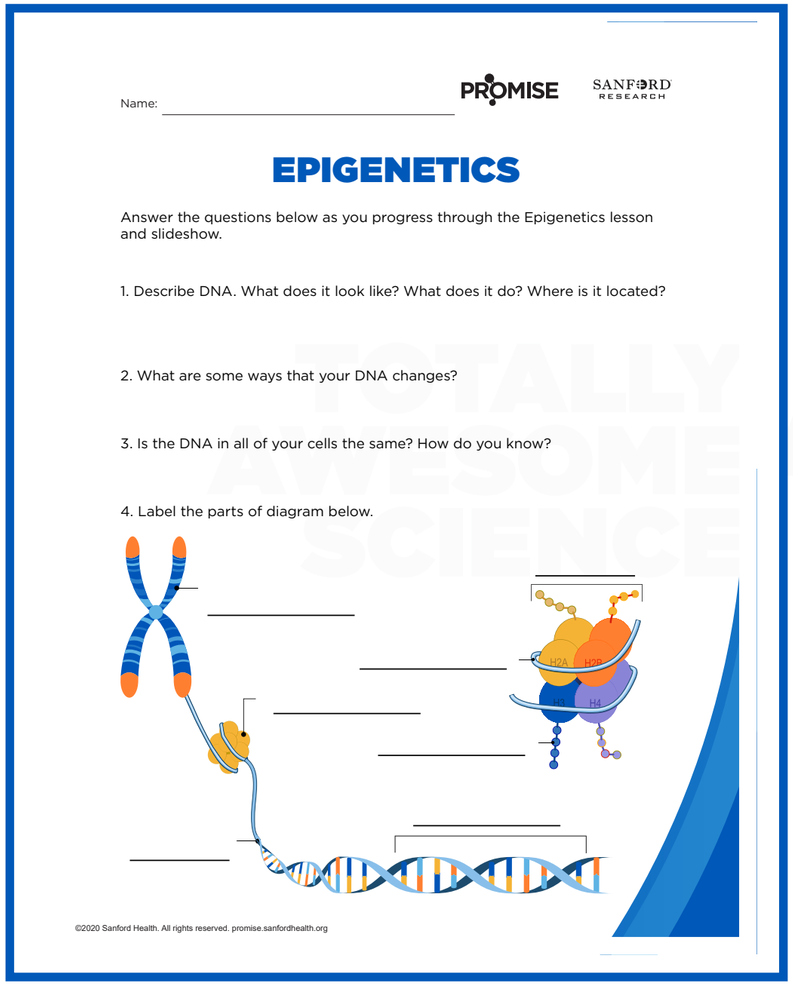
Adam and Patrick are monozygotic twins (identical) and share identical DNA. The boys grew up in the same household, went to the same school, and lived fairly “normal” childhoods. However, when Patrick turned 30, doctors found that he had developed a type of colon cancer.

CASE STUDY

Adam wanted to see if he would also have the same cancer as his twin. Adam's results came back negative for any type of cancer.

How is it possible that only one of the twins (sharing 100% of their DNA) developed this disease?

THINK | PAIR | SHARE



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EPIGENETICS

Answer the questions below as you progress through the Epigenetics lesson and slideshow.

1. Describe DNA. What does it look like? What does it do? Where is it located?

2. What are some ways that your DNA changes?

3. Is the DNA in all of your cells the same? How do you know?

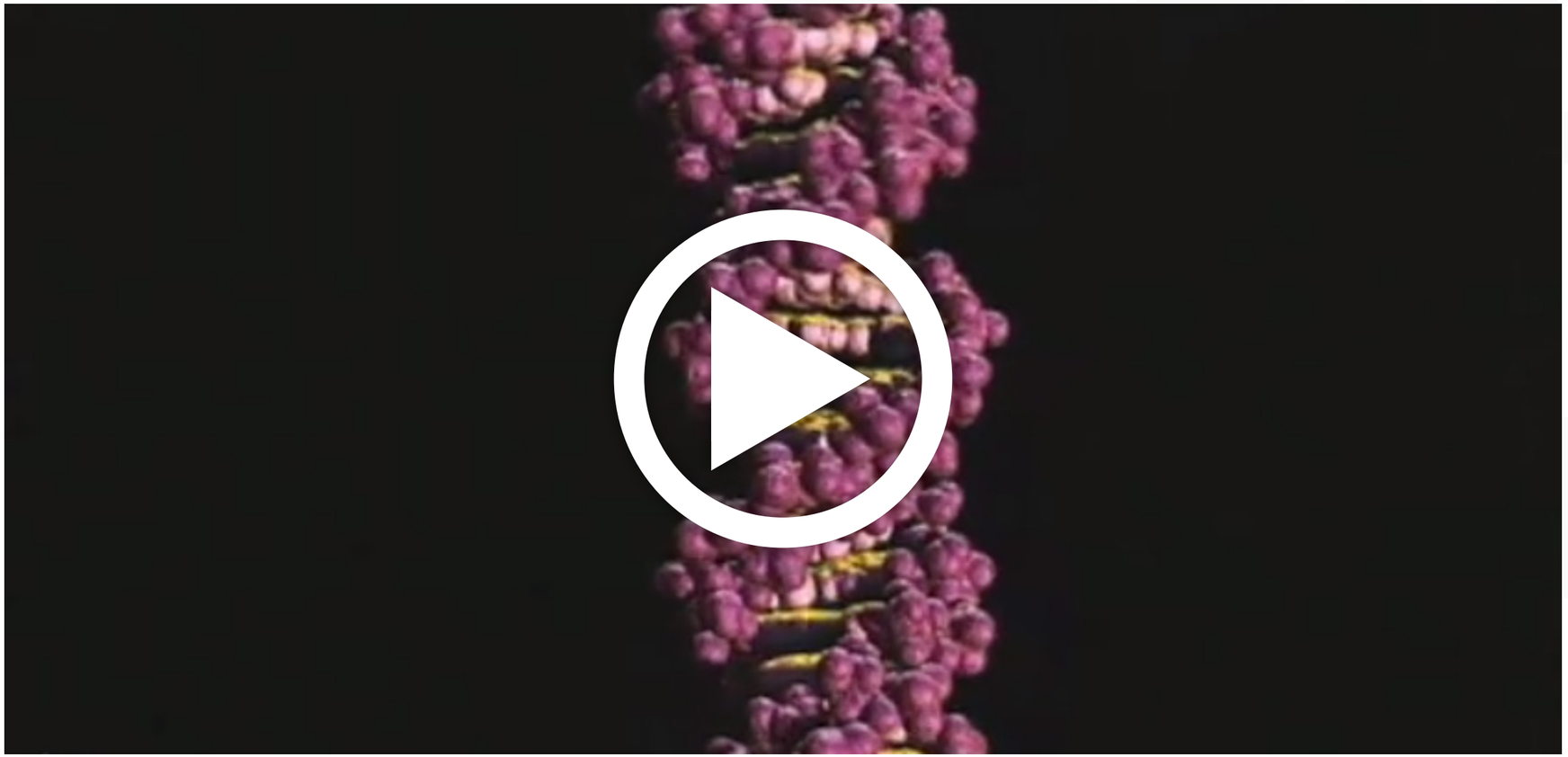
4. Label the parts of diagram below.

- Get a partner.
- Answer the questions in your lab notebook.
- Share your answers with the class.

WHAT IS DNA?

- DNA provides a “blueprint” of all the things that make up your body
- All cells in our body have the same DNA, even though they are so different
- Central Dogma of Biology

WATCH THIS!



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TRANSCRIPTION & TRANSLATION

The goal of this activity is to transcribe and translate this DNA sequence to a polypeptide (protein). This DNA sequence belongs to a zebrafish. Zebrafish are important to research because they share 70% of their genes with humans.

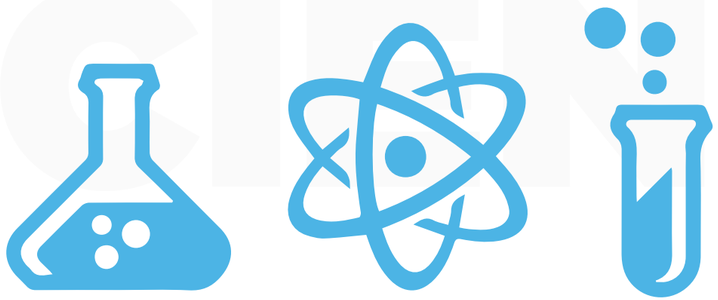
STEP 1: Transcribe DNA to RNA. A > U; T > A; C > G; G > C

STEP 2: Translate RNA to amino acids using the codon box below. Record the single letter for the amino acid in the mRNA box.

STEP 3: Use the table to decide which protein you made.

	U	C	A	G	
U	UUU, UUC – Phe - F UUA, UUG – Leu - L	UCU, UCC, UCA, UCG – Ser - S	UAU, UAC – Tyr - Y **UAA Stop** **UAG Stop**	UGU, UGC – Cys - C **UGA Stop** UGG – Trp - W	U C A G
C	CUU, CUC, CUA, CUG – Leu - L	CCU, CCC, CCA, CCG – Pro - P	CAU, CAC – His - H CAA, CAG – Gln - Q	CGU, CGC, CGA, CGG – Arg - R	U C A G
A	AUU, AUC, AUA – Ile - I **AUG Met - M**	ACU, ACC, ACA, ACG – Thr - T	AAU, AAC – Asn - N AAA, AAG – Lys - K	AGU, AGC – Ser - S AGA, AGG – Arg - R	U C A G
G	GUU, GUC, GUA, GUG – Val - V	GCU, GCC, GCA, GCG – Ala - A	GAU, GAC – Asp - D GAA, GAG – Glu - E	GGU, GGC, GGA, GGG – Gly - G	U C A G

FEELING STUCK? TRY THIS!

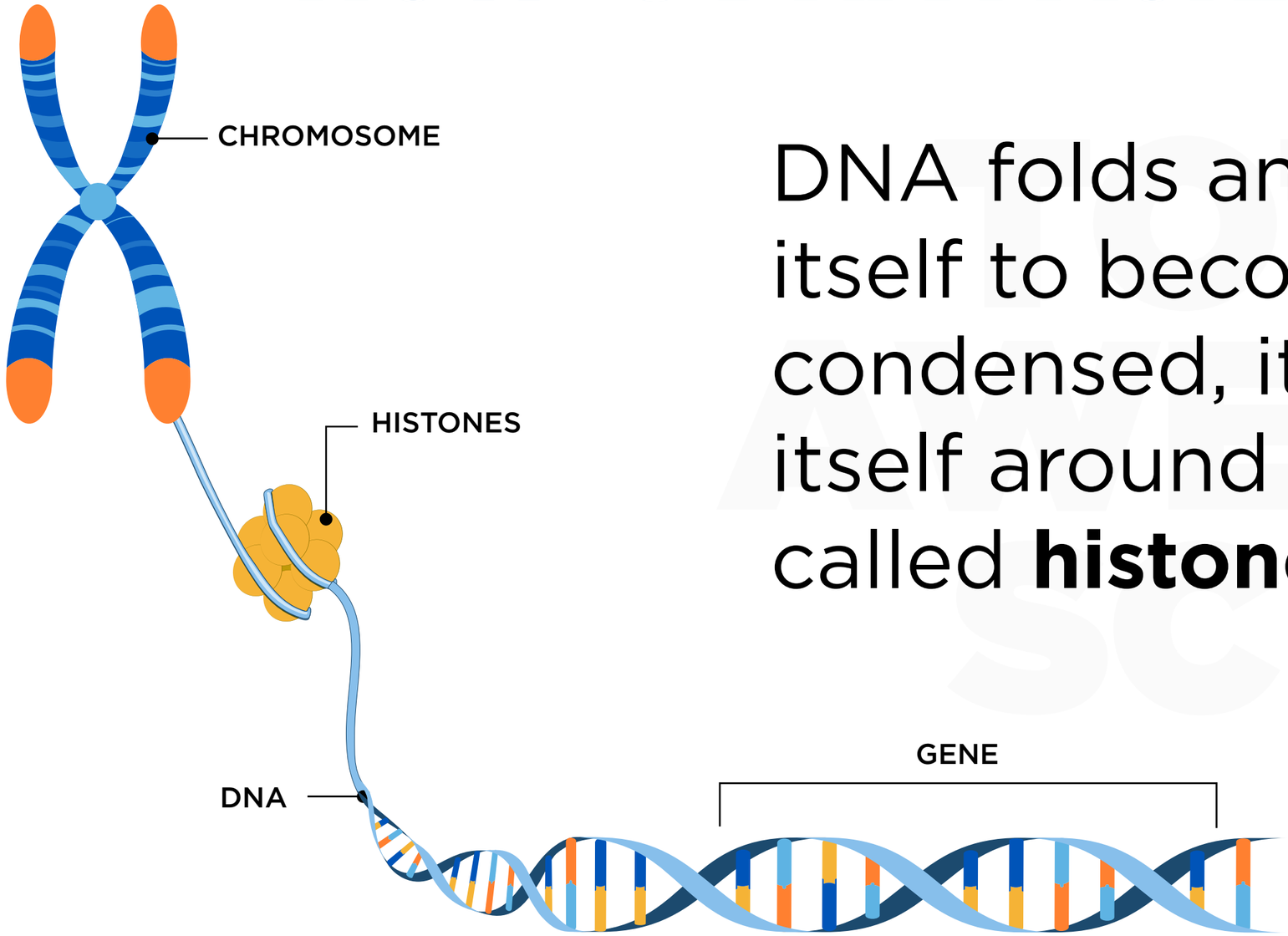


HOW IS DNA PACKAGED?

We have enough DNA in all our cells to stretch to the moon and back 51 times (about 6 feet per cell)!

How can we fit this all into one cell?

HOW IS DNA PACKAGED?

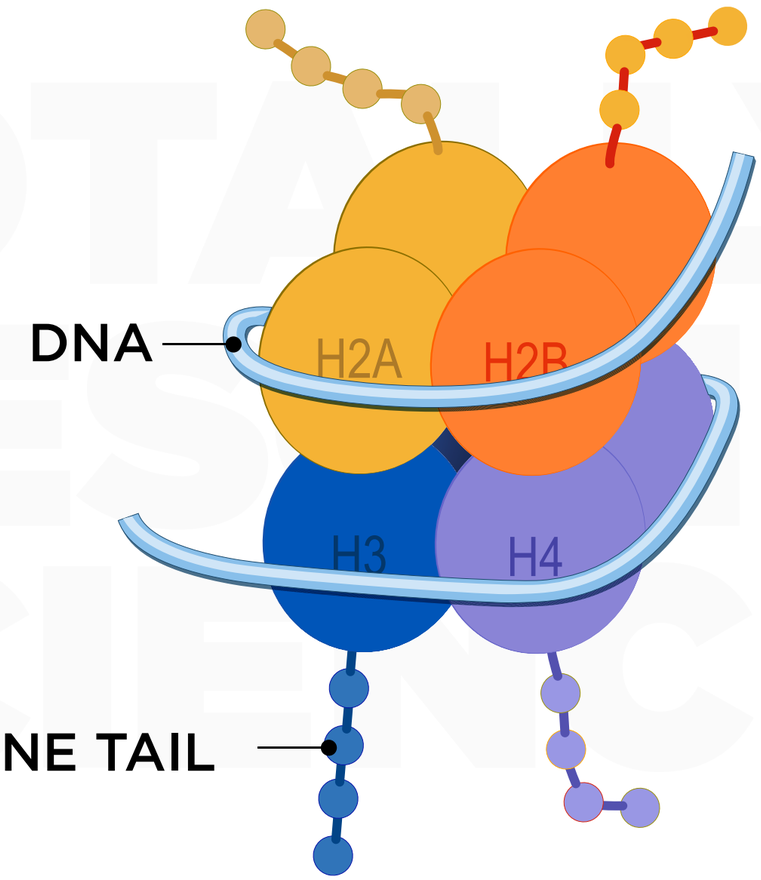


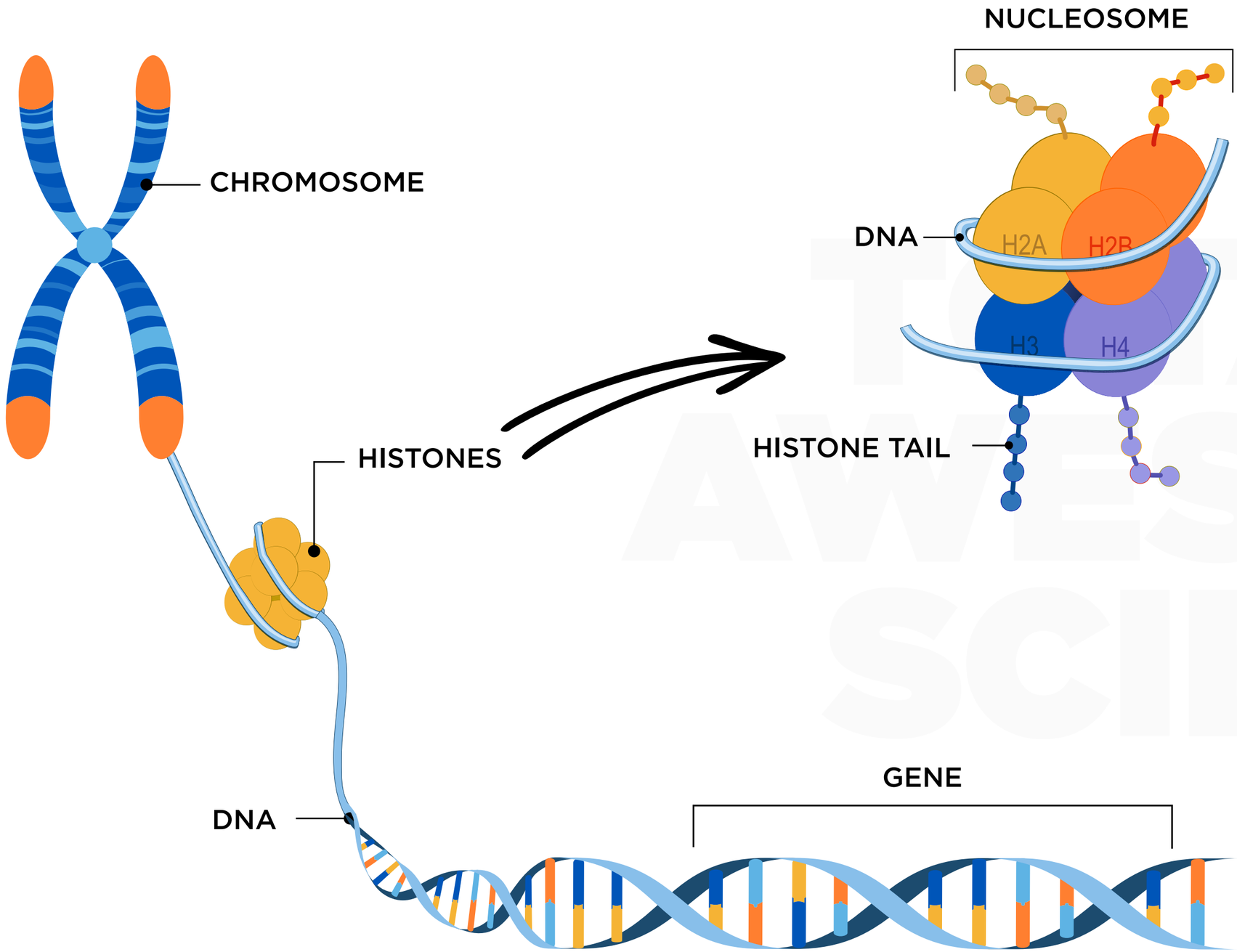
DNA folds and coils on itself to become more condensed, it then wraps itself around proteins called **histones**.

HOW IS DNA PACKAGED?

When DNA is very tightly packaged around histones, it is called **heterochromatin** and is mostly “inactive.”

When DNA is more loosely packaged around histones, it is called **euchromatin** and is mostly “active.”





Histones are positive in nature, DNA is negative in nature.

WHAT CONTROLS HOW TIGHTLY DNA IS PACKAGED?

- Epigenetics
  - Epi- means on top of, or over.
- Epigenetics are modifications that affect how the DNA is packaged and therefore changes how much a gene is expressed (if at all).
  - This **does not** change the code (A, T, C and Gs) of your DNA.

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Unlike genetic changes, epigenetic changes ARE NOT permanent.

LET'S EAT, GRANDMA!

The letters are the same, but the addition of punctuation changes the meaning.

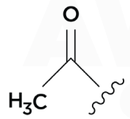
LET'S EAT GRANDMA!

GENETIC OR EPIGENETIC?

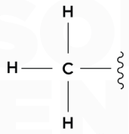
5. Fill out the table below with “yes” or “no” to record whether the change is genetic or epigenetic.

	Genetic Change	Epigenetic Change
Caused by nucleotide sequence change		
Caused by change in DNA packaging		
Irreversible		
Reversible		
Can cause disease		
Changes how DNA sequences are read		

6. Circle the correct answers under each figure.



Acetyl groups generally **(tighten/loosen)** DNA which **(increases/decreases)** expression.



Methyl groups generally **(tighten/loosen)** DNA which **(increases/decreases)** expression.

7. What are some things that can change epigenetic marks?

8. Should Adam be concerned for future cancers? Why or why not? What do you think a doctor would recommend to Patrick?

Fill out the chart in your lab notebook with “yes” or “no” depending on whether the change is genetic or epigenetic.

WHAT ARE EPIGENETIC MARKS?

- Acetylation, Methylation, & more!
- Epigenome is your unique combination of these modifications.
- These modifications change how tightly or loosely regions of your DNA are packaged.
- This changes the amount of gene transcript that gets made.

BUILD A HISTONE

Materials Needed:

- Scissors
- Paper Clips
- Tape



1. Cut on the dotted lines to separate all pieces on the following pages (DNA strands, histones, acetyl groups, methyl groups, RNA polymerase)
2. Fold the histone along the vertical solid lines and then tape the ends of the histone together. Histones help condense DNA into even smaller units. Histones have an overall positive charge and DNA has an overall negative charge. Note that histones are made of eight subunits (2 of each H2A, H2B, H4 and H3) called an octomer.
3. Tape the DNA strands together to create one, long strand.
4. Wind the DNA strand around the histones, securing part of the DNA with a paperclip. The regions of DNA that are wound around the histone are called euchromatin, which is inactive DNA. The section of DNA between the two histones is called heterochromatin and is transcribed.
5. Place the RNA polymerase on the exposed DNA strand. RNA polymerase in the cell is accompanied by many other helper proteins.
6. First, add a acetyl group onto a histone tail. Using what you learned in the epigenetics lesson, demonstrate what would happen. Next, remove the acetyl group and add a methyl group. How would this change how the DNA is packaged? Demonstrate both to your neighbor.

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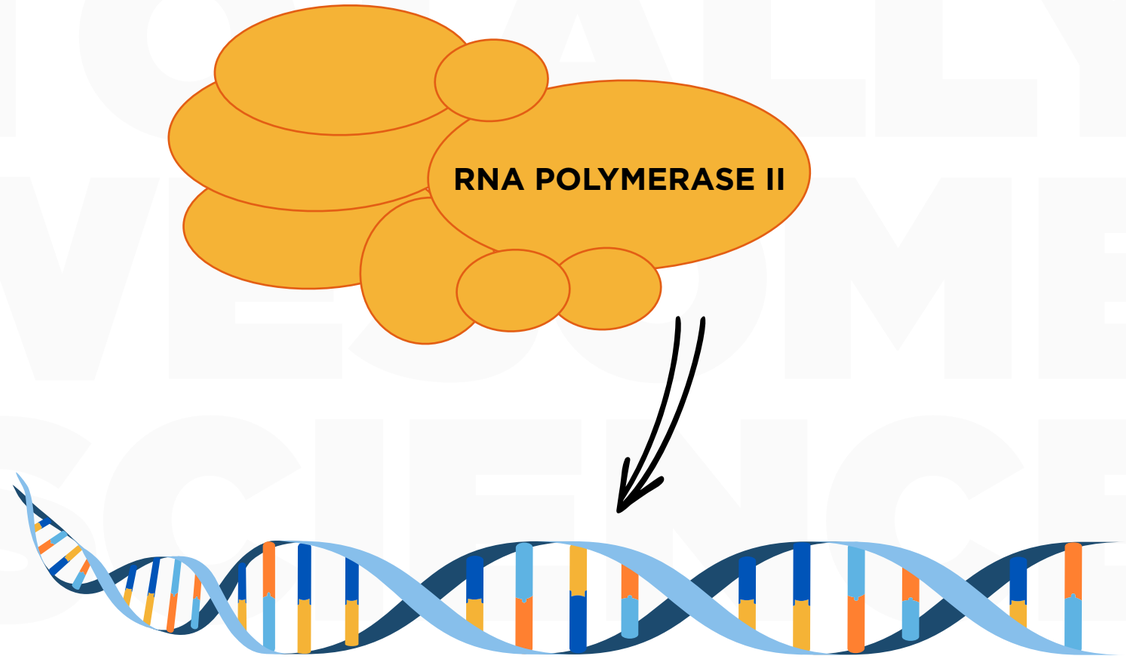
BUILD A HISTONE!

Follow the instructions on the student handout to build your own histone.

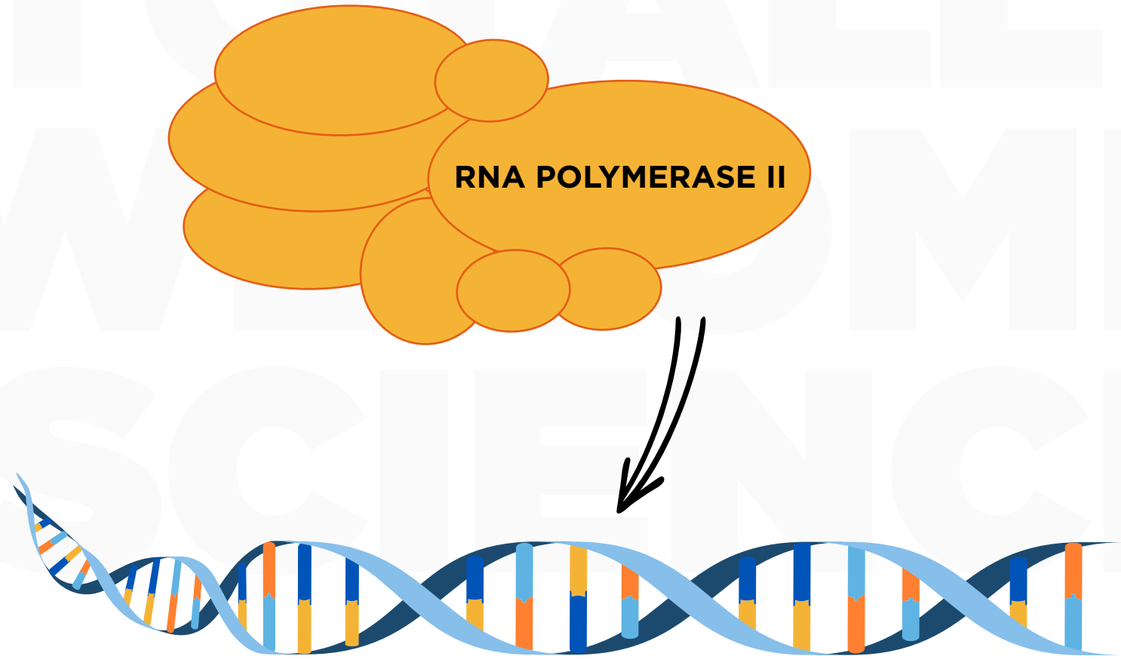
DO MARKS CHANGE GENE EXPRESSION?

Acetylation of histone tails is correlated with increased transcription. Chromatin is loosened and transcription machinery is drawn to the DNA.

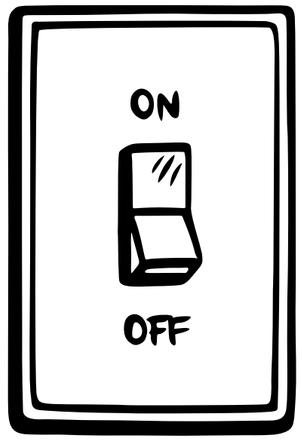


DO MARKS CHANGE GENE EXPRESSION?

Histone methylation is correlated with repressed transcription. Chromatin is tightened and transcription machinery cannot attach the DNA.



MORE THAN JUST ON OR OFF



Epigenetics can turn genes on and off but they can also adjust the amount of protein necessary depending on the needs to the cell. The necessary amount of a certain protein may change with:

- Time of development
- Energy expenditure
- Time of day
- Cell type

CHANGING EPIGENETICS

What are some things that change our epigenetics?

- Time of human development
- Signals received from neighboring cells
- Diet
- Stress
- Pollution
- Medications
- Drugs/Alcohol consumption

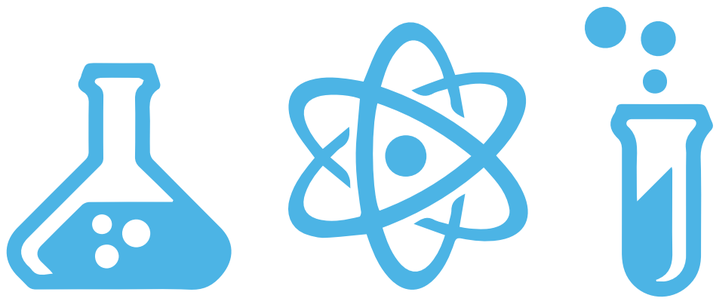
CASE STUDY

So what are some reasons that Patrick may have developed cancer and not Adam?

CASE STUDY

When Patrick and Adam left for college, Patrick went to a college in an industrial town with a lot of factories in it. Adam went to a college in a small town that focused mostly on farming. Patrick worked a high stress job and ate lots of processed foods due to time constraints. Adam also worked a lot but took up meditating to help with stress and indulged in fast food only on Fridays.

ANSWER THE QUESTIONS ABOUT ADAM & PATRICK IN YOUR LAB NOTEBOOK!



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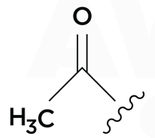

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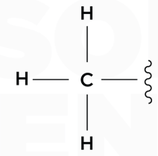

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EPIGENETICS PART 2

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EPIGENETICS REVIEW

Describe what DNA is (structure/function) and how it is packaged in the cell.

What is epigenetics and what does it do?

What kinds of things change epigenetics?

THINK | PAIR | SHARE

Based on what you learned so far, would you predict these changes to be heritable? Why or why not?

JIGSAW ACTIVITY

- Grab your Epigenetics Jigsaw.
- You will be assigned a color.
- Read the disease study of your assigned color.

JIGSAW ACTIVITY

- Meet with the other people who read the same case study.
- Discuss what you read and anwser the questions following your reading.

JIGSAW ACTIVITY

- Return to your original seat and discuss your disease study with those around you.
- Pay attention! You are responsible for their information as well as your own.

ARE EPIGENETICS HERITABLE?

Scientists have debated on whether some epigenetic changes are hertiable for years.

As of now, there is no consensus on the extent to which epigenetics are heritable.

ARE EPIGENETICS HERITABLE?

What is known, is that during our lifetime, many important epigenetic marks are:

1. Temporary based on the needs of the body and time of development.

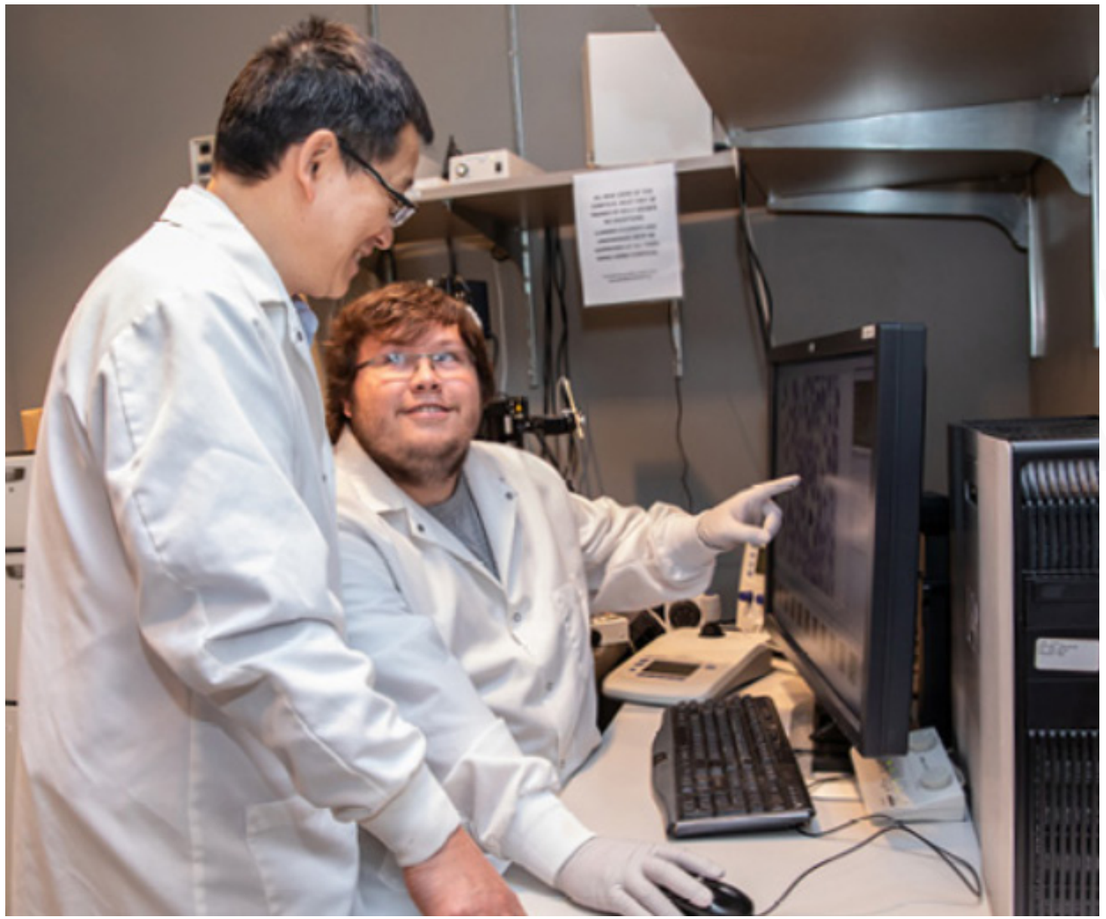
2. Dynamic and changing based on stress, diet, and environmental conditions among other things.

EPIGENETICS & DISEASE

It is also known that epigenetic changes can play a large role in the development of diseases such as:

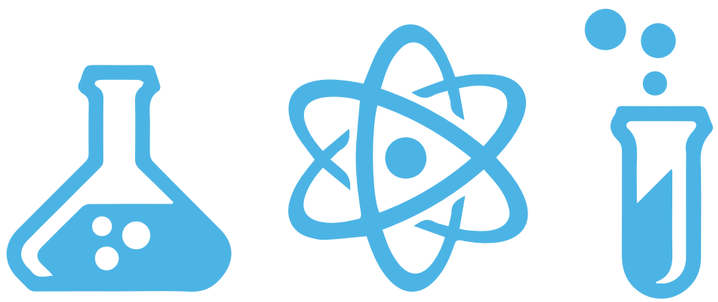
- Schizophrenia
- Autism
- Cancer
- Angelman’s Syndrome

EPIGENETICS AT SANFORD



You could help find the answers! The Tao lab at Sanford Research studies epigenetic changes in patients with osteosarcoma.

ANSWER THE REMAINING QUESTIONS IN YOUR LAB NOTEBOOK!



C. Some say that hearing the stories of tragedies like above from parents cause PTSD like symptoms in children. How, if you had everything at your disposal, could you test this?

Epigenetics of Maternal Care & Stress Management

A. What was the outcome of rat pups who were nurtured more? How were they different than those that were neglected?

B. Do you think the behavior of the rat pups would switch if you swapped them a second time? Why or why not?

C. What evidence supports that these epigenetic marks can be passed on to offspring? What evidence goes against it?

Critiques & Questions About Inheritance

A. What might explain epigenetic similarities found between parent and offspring if epigenetic marks are not heritable? For example, why might a mom and daughter both have a higher risk for diabetes if it is not passed down in the epigenome?

B. How many people do you think should be surveyed in order to make a conclusion on epigenetic inheritance?

C. If all scientific equipment and money was available to you, how could you design a study to test this?