

Title	"Above" DNA: An Exploration of the Epigenome
Introduction	<p>Epigenetics is a relatively new branch of biology and biochemistry. Literally translating to "above the genome," epigenetics examines the role that external/environmental factors serve in controlling the expression of an individual's genes. This unit plan is designed to serve as an introduction to epigenetics and a survey of relevant applications to disease, biotechnology, and cellular functions.</p> <p>The unit spans approximately 1 week in a traditional (50-minute period) high school Biology (9th, 10th grade) classroom. The activities can be amended to increase the rigor for AP-level students. The main components are 1) Review of Genetics and an Overview of Epigenetics, 2) Histone Action Simulation, and 3) a Final Assessment, educating community members about epigenetics.</p>
Real Science Application	<p>The Strahl lab has been engaged in a large-scale, high-throughput proteomics project to uncover the function of histone modifications using peptide arrays.</p> <p>Since initiating this project, they have shown how a number of effector proteins are influenced by combinatorial histone post-translational modifications (PTMs). They are also collaborating with a wide number of labs across the world to decipher the binding potential of newly identified histone "reading" proteins.</p> <p>One area of particular interest is how adjacent or paired domains in chromatin-associated protein interpret the 'histone code'. Recent studies from their lab have shown that the tandem Tudor (TTD) and adjacent PHD domains of UHRF1, an E3 ubiquitin ligase domain-containing protein, function in unison to bind a specific heterochromatic signature of H3 for its chromatin recruitment and DNA methylation maintenance function (see Rothbart...Strahl, 2013 Genes & Development, 27:1288-98). These studies highlight an important feature of how histone-associated proteins engage chromatin, and the Strahl lab notes that many other chromatin-associated proteins also contain paired "docking" domains similar to UHRF1. A future goal will be to define the interactions and downstream biological functions of these multi domain-containing proteins.</p>
Curriculum Alignment	<p><u>NCSCOS Biology Objectives</u></p> <p>Bio.1.1 Understand the relationship between the structures and functions of cells and their organelles.</p>

	<ul style="list-style-type: none"> • Bio.1.1.3 Explain how instructions in DNA lead to cell differentiation and result in cells specialized to perform specific functions in multicellular organisms. <ul style="list-style-type: none"> ○ Explain that multicellular organisms begin as undifferentiated masses of cells and that variation in DNA expression and gene activity determines the differentiation of cells and ultimately their specialization. ○ During the process of differentiation, only specific parts of the DNA are activated; the parts of the DNA that are activated determine the function and specialized structure of a cell. ○ Different parts of the genetic instructions are used in different types of cells, influenced by the cell's environment and past history. <p>Bio.3.1 Explain how traits are determined by the structure and function of DNA.</p> <ul style="list-style-type: none"> • Bio.3.1.1 Explain the double-stranded, complementary nature of DNA as related to its function in the cell. <ul style="list-style-type: none"> ○ With few exceptions, all cells of an organism have the same DNA but differ based on the expression of genes. <p><u>Next Generation Science Standards: High School Life Science</u></p> <p>HS-LS1-1. Construct an explanation based on evidence for how the structure of DNA determines the structure of proteins which carry out the essential functions of life through systems of specialized cells.</p> <ul style="list-style-type: none"> • LS1.A: Structure and Function <ul style="list-style-type: none"> ○ Systems of specialized cells within organisms help them perform the essential functions of life. (HS-LS1-1) ○ All cells contain genetic information in the form of DNA molecules. Genes are regions in the DNA that contain the instructions that code for the formation of proteins, which carry out most of the work of cells. (HS-LS1-1) <p>HS-LS3-1. Ask questions to clarify relationships about the role of DNA and chromosomes in coding the instructions for characteristic traits passed from parents to offspring.</p>
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	<ul style="list-style-type: none"> • LS3.A: Inheritance of Traits <ul style="list-style-type: none"> ○ Each chromosome consists of a single very long DNA molecule, and each gene on the chromosome is a particular segment of that DNA. The instructions for forming species' characteristics are carried in DNA. All cells in an organism have the same genetic content, but the genes used (expressed) by the cell may be regulated in different ways. Not all DNA codes for a protein; some segments of DNA are involved in regulatory or structural functions, and some have no as-yet known function. (HS-LS3-1) • LS3.B: Variation of Traits <ul style="list-style-type: none"> ○ Environmental factors also affect expression of traits, and hence affect the probability of occurrences of traits in a population. Thus the variation and distribution of traits observed depends on both genetic and environmental factors. (HS-LS3-2),(HS-LS3-3) <p><u>Optional: AP® Biology Standards</u></p> <p>Essential Knowledge 2.E.1: Timing and coordination of specific events are necessary for the normal development of an organism, and these events are regulated by a variety of mechanisms.</p> <ul style="list-style-type: none"> a. Observable cell differentiation results from the expression of genes for tissue-specific proteins. <p>Essential Knowledge 3.B.1: Gene regulation results in differential gene expression, leading to cell specialization.</p> <ul style="list-style-type: none"> c. In eukaryotes, gene expression is complex and control involves regulatory genes, regulatory elements, and transcription factors that act in concert. d. Gene regulation accounts for some of the phenotypic differences between organisms with similar genes. <p>Essential Knowledge 3.B.3: A variety of intercellular and intracellular signal transmissions mediate gene expression.</p> <ul style="list-style-type: none"> a. Signal transmission within and between cells mediates gene expression.
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Learning Outcomes	<ul style="list-style-type: none"> • Participants will define the term “epigenetics” • Participants will identify the components of chromatin • Participants will describe how gene expression can vary among individuals that are genetically identical • Participants will compare and contrast genetics and epigenetics • Participants will understand and model the role of histones in gene expression • Participants will use technology to educate community members (laypeople) about epigenetics; presentation may be persuasive or informative
Time Required and Location	<p>This unit is designed to extend over the course of 1 week, and supplement the gene expression and/or protein synthesis portion of the Molecular Genetics unit in a traditional 50-minute biology or honors biology classroom. All activities take place in the classroom, with the exception of the final assessment, which may take place elsewhere, as it requires involvement of community members. Activities and vocabulary requiring increased rigor may also supplement this unit plan if the content is to be used in an AP Biology® classroom.</p>
Materials Needed	<p>Facilitator List</p> <ul style="list-style-type: none"> • “Overview of Epigenetics” Power Point presentation • Rubric for grading community engagement assessments <p>Participant List</p> <ul style="list-style-type: none"> • Student Worksheet: “Life as we knew it: Introduction to Epigenetics” • <u>Optional</u>: Copies of <i>The Epigenetics Revolution</i> by Nessa Carey (or access to copies of chapters 2 and 3) • Access to a tablet, smartphone, or laptop • Histone Model Materials: <ul style="list-style-type: none"> ○ Biology/Honors Biology: <ul style="list-style-type: none"> ▪ Epigenetics Handout and follow-up homework sheet ▪ Permanent marker ▪ Ballpoint pen ▪ 3 pieces of thin (small-diameter) rubber surgical

	<p>tubing or bungee cord; 24" long, each</p> <ul style="list-style-type: none"> ▪ 2 small binder clips ▪ Packing/Duct tape <p>○ AP® Biology:</p> <ul style="list-style-type: none"> ▪ DNA/Histone Model Handout, modified from Utah Genetics ▪ Scissors ▪ Tape ▪ Paperclips <ul style="list-style-type: none"> • 3 sheets of construction paper for Power Point Foldable • Instructional handout and rubric for community engagement assessment
Safety	There are minimal safety concerns for this unit.
Participant Prior Knowledge	<p>These activities are designed to supplement the gene expression and/or protein synthesis portion of the Molecular Genetics unit in a high school biology classroom. Participants should have a working knowledge of the structure and function of DNA, protein synthesis, and cell differentiation.*</p> <p>Participants should be familiar with the following terminology:</p> <ul style="list-style-type: none"> • Deoxyribonucleic Acid (DNA) • Chromosome • Gene • Gene Expression • Nitrogenous base • Nucleotide • Transcription • Translation <p>*If this unit plan is being implemented in an AP® Biology course, students should also understand post-transcriptional modifications such as acetylation, methylation, etc., histones, and the differences between heterochromatin and euchromatin.</p>

Facilitator Preparations	<p>In order to be effectively prepared for questions and class discussion, it is suggested that the instructor complete the following tasks before the beginning of the unit:</p> <ul style="list-style-type: none"> • Familiarize yourself with the online quiz game program, Kahoot • If you are unfamiliar with Epigenetics, consider reading <i>The Epigenetics Revolution</i> by Nessa Carey, ahead of time, in order to be prepared for classroom discussion. • Research some common examples of epigenetic research: <ul style="list-style-type: none"> ○ Agouti Mouse ○ Diseases linked to epigenetics ○ The role of histones in epigenetics ○ Dutch Hunger Famine ○ Bees and “royal jelly” ○ Daphnia “helmets” ○ Behavioral links to epigenetics • Familiarize yourself with the epigenetics resources available from Utah Genetics and PBS NOVA • Become familiar with online resources that can be used for: <ul style="list-style-type: none"> ○ The Community Engagement Assessment <ul style="list-style-type: none"> ▪ PowToon ▪ Aurasma ▪ YouTube ▪ Prezi • Be familiar with use of online journals and Google Scholar. You may also consider spending a day with students (whether during this unit or earlier in the school year) teaching them how to do research and avoid plagiarism. Your media center/technology person may be able to assist in organizing a session like this. • Talk with other teachers, scientists, community members, etc. about having your students present their Community Engagement Assessments to their classroom or group. • Create rubrics for each of the graded assignments.
Activities	Day 1: Review/Reading Day (50 minutes)

	<p>At this point in time, participants should already be familiar with the structure and function of DNA, the processes of transcription and translation, and the concept of cell differentiation.</p> <p>The instructor may consider having participants complete a quick review quiz on Kahoot to demonstrate mastery of previous topics. This simply requires the teacher to set up an account with Kahoot and provide participants with the participation code. Alternatively, the instructor may provide participants with a copy of the “Life as we Knew it” worksheet, if access to technology is unavailable. [10 minutes]</p> <p>As a warm-up (and to review content from the previous unit), have participants (in groups of 3-4) create a KWL chart. Participants should include information about what they know about genetics, what they want to know about epigenetics, and then save the “what they learned” portion until the end of the unit. While reviewing the answers for warm-up, be sure to go over the following terms. Discuss any questions or misconceptions that arose during the participants’ independent reading time. The reading refers to DNA as a script to a play. Ask participants what other documents may be analogous to the function of DNA (recipe, computer code, instruction manual):</p> <ul style="list-style-type: none"> • Gene • Gene expression • Transcription • Translation <p>As participants finish their charts, the instructor should segue into a discussion that centers on the analogy the genetics is like the script to a play. The text, itself, does not change; it serves as the instructions for the play’s implementation. However, epigenetics describes how the script is interpreted by individual actors (tone, facial expression, movement, etc.). The instructor may want to illustrate this example by having participants read the same passage or monologue from a play, and instructing participants to read it in two different ways. This analogy is an easy way to demonstrate the concept of epigenetics, without including complex vocabulary. [25-30 minutes]</p> <p>In the remaining minutes of class, the instructor may begin the Overview of Epigenetics presentation (guided notes) or assign a reading to follow up the day’s discussion. Suggested readings include articles on epigenetics or chapter 3 of <i>The Epigenetics Revolution</i>: “Life as we know it now.” A quick discussion of the assigned reading can be used as the warm-up on day 2. [5-10 minutes]</p> <ul style="list-style-type: none"> • Suggested readings/resources:
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- <http://learn.genetics.utah.edu/content/epigenetics/>
- <http://www.whatisepigenetics.com/fundamentals/>
- <http://www.economist.com/blogs/economist-explains/2013/07/economist-explains-7>

Day 2: Overview of Epigenetics and Epigenetics Foldable (50 minutes)

As participants come into the classroom, they should try to answer the question on the board, “What is Epigenetics?” After writing the definition in their own words, the instructor should ask participants for their answers and try to make a “class-wide” definition. This discussion should segue into a presentation, given by the teacher, that highlights the basics of epigenetics, key players involved (e.g. histones, chromatin), and a few groundbreaking examples of epigenetics (e.g. Agouti mouse, Dutch Hunger Famine). [10-15 minutes]

See “Overview of Epigenetics” Power Point for specific information, images, and presentation notes.

Because taking notes from a Power Point is not the most effective way to engage participants, the facilitator should strongly consider having participants create a product (such as a foldable) from the Power Point presentation. A foldable is a participant-constructed manipulative (booklet) that can be used for organizing notes and ideas. Using 3 sheets of paper, participants should stagger the sheets, resulting in a booklet with 1 title tab and 5 topic tabs (one for each major topic in the presentation). Title: Epigenetics; Tab 1: What is it?; Tab 2: Chromatin/Histones; Tab 3: Epigenetics Modifications (divide tab in half—one side for histone acetylation, one side for DNA methylation); Tab 4: Epigenetics and Cell Differentiation; Tab 5: Famous Examples (divide in half—one side for Dutch Hunger Winter, one side for Agouti Mice). By engaging with the material, participants are more apt to remember the details of epigenetics and be able to apply them in later contexts. [35-40 minutes]

Day 3: All About Histones (50 minutes)

Today, participants will learn, in more detail, about the structure and role of histones in transcription and gene expression. Students will begin by watching a video from Utah Genetics, entitled, [“The Epigenome at a Glance.”](#) The video discusses the roles and modifications of histones in gene expression, as well as cell differentiation. After watching the video, the instructor may discuss the link between chromatin density and transcription accessibility. He/She may also highlight the consequences

	<p>that occur when the epigenome is modified incorrectly. [5-10minutes]</p> <p>*For AP® Biology students, the instructor may also discuss post-translational modifications to the chromatin, such as histone acetylation or DNA methylation.</p> <p>If participants have tablets, smart phones, and/or laptops, the instructor should also encourage them to explore Utah Genetics' "Gene Control" page and 1) change the settings on the "control knob", 2) Read the "Could You Really Do This?" section, and 3) Learn about "Gene Control and Cancer." If participants do not have access to such technology, the instructor may guide them through this webpage. [10 minutes]</p> <p>During the last half of class, participants will model the action of histones in the epigenome.* Using a worksheet from PBS NOVA, participants will use small-diameter surgical tubing (or bungee cords) to visually represent condensed and de-condensed chromatin. The worksheet also includes a set of discussion questions that could be answered for homework. The original lesson plan with objectives can be found here. [25-30 minutes]</p> <p>*The PBS NOVA histone modeling activity may be too simple for an AP® Biology classroom. For an in-depth model and discussion of histone acetylation and DNA methylation, the Utah Genetics "DNA and Histone Model" may better serve the needs of AP® students.</p> <p>Days 4-5: Assessment</p> <p>See "Assessment" Section below.</p>
Assessment (Required)	<p>Community Engagement Assessment (2 in-class days):</p> <p>The best way to evaluate participants is to have them explain it to others. More specifically, if a participant can explain complex scientific phenomena in a way that laypeople can understand, it means that they have thoughtfully evaluated their own understanding, in order to make the information more accessible to others. This assessment not only strives to demonstrate mastery of epigenetics, but also to engage members of the community—whether that is other students, their parents, or community members.</p> <p>To demonstrate mastery of epigenetics, participants will develop an educational video, module, tutorial, or classroom lesson that they will then present to members of the public (outside the biology classroom). Projects will explain complex biochemical phenomena using terminology that everyone can understand: from middle school through adulthood. Essentially, participants will be providing:</p>

	<ul style="list-style-type: none"> • An overview of epigenetics • Comparison of the genome and epigenome • A spotlight on a particular epigenetic scenario or case study that is relevant and valuable for community members <ul style="list-style-type: none"> ○ <i>It may serve the community best to discuss an epigenetic concept with implications for human health</i> ○ <i>Participants may draw upon the In-Class Inquiry research done by their peers</i> <p>Presentation method is at the discretion of the participant. The presentation may serve as an information session, or be framed as a persuasive argument. If groups of participants want to work together, they must seek approval from the instructor. Some suggested methods for presentation are listed below:</p> <ul style="list-style-type: none"> • PowToon • Aurasma • YouTube • Prezi <p>Other presentation methods will require approval from the instructor.</p> <p>This assessment is worth 2 grades: <u>one</u> for developing the educational materials and <u>one</u> for presenting the project to a group of at least 3 individuals.</p> <p>Rubrics will be used for assessing the participant's:</p> <ul style="list-style-type: none"> • Detailed explanation of epigenetics • Comparison of the genome and epigenome • Thorough analysis of an epigenetic case study or concept • Use of presentation technology • Organization of his/her instructional materials • Evidence of presentation to a group of community members
Critical Vocabulary	<p>The following list of terms demonstrates critical concepts that participants need to know in order to meet the learning outcomes for this project.</p> <p>For Biology and Honors Biology Students:</p>

	<ul style="list-style-type: none"> • Epigenetics: The study of external and environmental factors that turn genes on and off and affect how cells read genes. • Histone: Proteins that are closely associated with DNA, and can be epigenetically modified. • Nucleosome: A combination of 8 histone proteins with DNA wrapped around them. • Chromatin: The combination of DNA wrapped around histone proteins. <p>For AP® Biology students:</p> <ul style="list-style-type: none"> • DNA Methylation: process by which methyl groups ($-\text{CH}_3$) are added to DNA (at a cytosine base). This typically results in decreased expression of a gene and decreased production of the resulting protein. • Acetylation: The addition of an acetyl group (COCH_3) to the “tail” of a histone. This typically results in a loosening of DNA around the histone, allowing for increased access by transcription factors, which leads to increased expression of the gene. • CpG Islands: A location along a strand of DNA where a cytosine nucleotide is followed by a guanine nucleotide. These “islands” may undergo methylation on the cytosine. • HDAC (Histone Deacetylase): An enzyme that can remove acetyl groups from histone proteins. • DNMT (DNA Methyltransferase): an enzyme that can add methyl groups to cytosine bases in DNA.
Community Engagement	<p>The assessment for this unit has, within its structure, a component of community engagement. To demonstrate mastery of epigenetics, participants will develop an educational video, module, tutorial, or classroom lesson that they will then present to members of the public (outside the biology classroom). Projects will explain complex biochemical phenomena using terminology that everyone can understand: from middle school through adulthood. Essentially, participants will be providing:</p> <ul style="list-style-type: none"> • An overview of epigenetics • Comparison of the genome and epigenome <p>Participants may choose to present their modules to another non-</p>

	<p>science class at their school, or travel to a middle school to present. Participants may also present to a group at their church, community center, or other public forum.</p> <p>As part of their grade, participants must do one of the following, to prove that they involved the community in their project:</p> <ul style="list-style-type: none"> • Invite the instructor to attend their presentation • Ask audience members to complete a student-constructed survey about the participant's presentation • Film/take pictures at the presentation event <p><i>It should be noted that, while the participant may finish his/her project by the assigned date, he/she should be allowed additional time to coordinate and present the module to the chosen community group. Alternatively, the instructor may consider presenting the community engagement assessment early in the unit to allow students time to plan their presentation.</i></p>
Extension Activities	<p>To differentiate the Community Engagement Assessment for honors and standard biology participants, the instructor may consider requiring honors participants to present their project to an audience outside of school, while standard participants may present for extra-credit. Additionally, if access to transportation or a presentation venue is an issue, the instructor may consider organizing a community science fair at the school. This format provides all students with the opportunity to present to the public.</p> <p>If there is additional time, the instructor may consider inviting former students (now in AP® Biology or studying at the university level) to attend a panel in which participants present their modules. If the instructor has connections with mentors or colleagues who teach similar content (whether at the high school or university level), he/she may consider hosting such a panel, while also allowing colleagues to discuss their experience/research with epigenetics.</p> <p>If the instructor finds that this community engagement assessment is a truly valuable experience and teaching tool, he/she may ask the participant to present his/her module at a local or statewide conference, thus broadening the scope of community engagement.</p> <p>For example, the instructor may consider having participants present their modules at a local science symposium, such as the NC Science Festival at UNC-Chapel Hill. Not only would participants share their curriculum with North Carolina science teachers, but they could also</p>

	explain (in their own terms), the concept of epigenetics to other children in attendance.
Modifications	For participants who struggle with access to technology, consider offering extra tutoring hours or sessions in the computer lab to allow participants the time necessary for developing their Community Engagement Assessments. If technology access is limiting a participant's success, the instructor may consider adapting the assignment to rely less heavily on use of technology.
Alternative Assessments	<p>If a participant's assignment is modified because of reading comprehension skills, the following alternative assessments may be used:</p> <ul style="list-style-type: none"> Community Engagement Assessment: Create a "dictionary" of the vocabulary that is necessary to understand the concepts associated with epigenetics. Work with a partner (who is completing the "full" version of the Community Engagement Assessment) and provide audience members with a copy of your dictionary before your partner begins his/her presentation. <p>If a participant's assignment is modified because of technological limitations, the following alternative assessments may be used:</p> <ul style="list-style-type: none"> Community Engagement Assessment: Develop course materials necessary to teach a group of individuals about epigenetics. Use as many, or as few technological tools as necessary.
References	<p>Carey, N. (2012). <i>The epigenetics revolution: How modern biology is rewriting our understanding of genetics, disease, and inheritance</i>. New York: Columbia University Press.</p> <p>Handouts:</p> <ul style="list-style-type: none"> "DNA & Histone Model" Handout is property of the Genetic Science Learning Center, University of Utah, http://learn.genetics.utah.edu "Epigenetics" handout from PBS NOVA was obtained from http://www.pbs.org/wgbh/nova/body/epigenetics.html <p>Websites:</p> <p>DNA Wrap: Packaging Matters</p> <p>University of Utah, Genetic Science Learning Center, Epigenetics</p> <p>NOVA scienceNOW: Epigenetics</p>

Comments	This unit plan was developed as a curriculum product for the Kenan Fellows Program. The intent is for students to learn about epigenetics, while also developing their communication skills, use of technology in presentations, and their ability to engage with members of the community.
Author Info	<p>In this section, tell us about yourself and your mentor! Include the following:</p> <p>Kenan Fellow: Brooke Sauer</p> <ul style="list-style-type: none"> • Durham School of the Arts, Durham, NC • 9-12, Biology and AP® Biology • 4 years teaching experience • Brooke.Sauer@dpsnc.net <p>Mentor: Dr. Brian Strahl</p> <ul style="list-style-type: none"> • Department of Biochemistry and Biophysics, UNC School of Medicine • Research Questions: <ul style="list-style-type: none"> ○ How do distinct chromosomal domains such as “euchromatin” and “heterochromatin” become established and maintained? ○ How is the underlying DNA within this highly compact and repressive chromatin environment made accessible to the protein complexes that utilize it? • Principal Investigator, Director of Graduate Studies, Faculty Director, <u>UNC High Throughput Peptide Synthesis and Array Core Facility</u> • brian_strahl@med.unc.edu

Assignment descriptions and rubrics can be found on subsequent pages, in the order in which they appear in this unit plan (Days 1-5).

Life as we *knew* it: Genetics Review

Name:

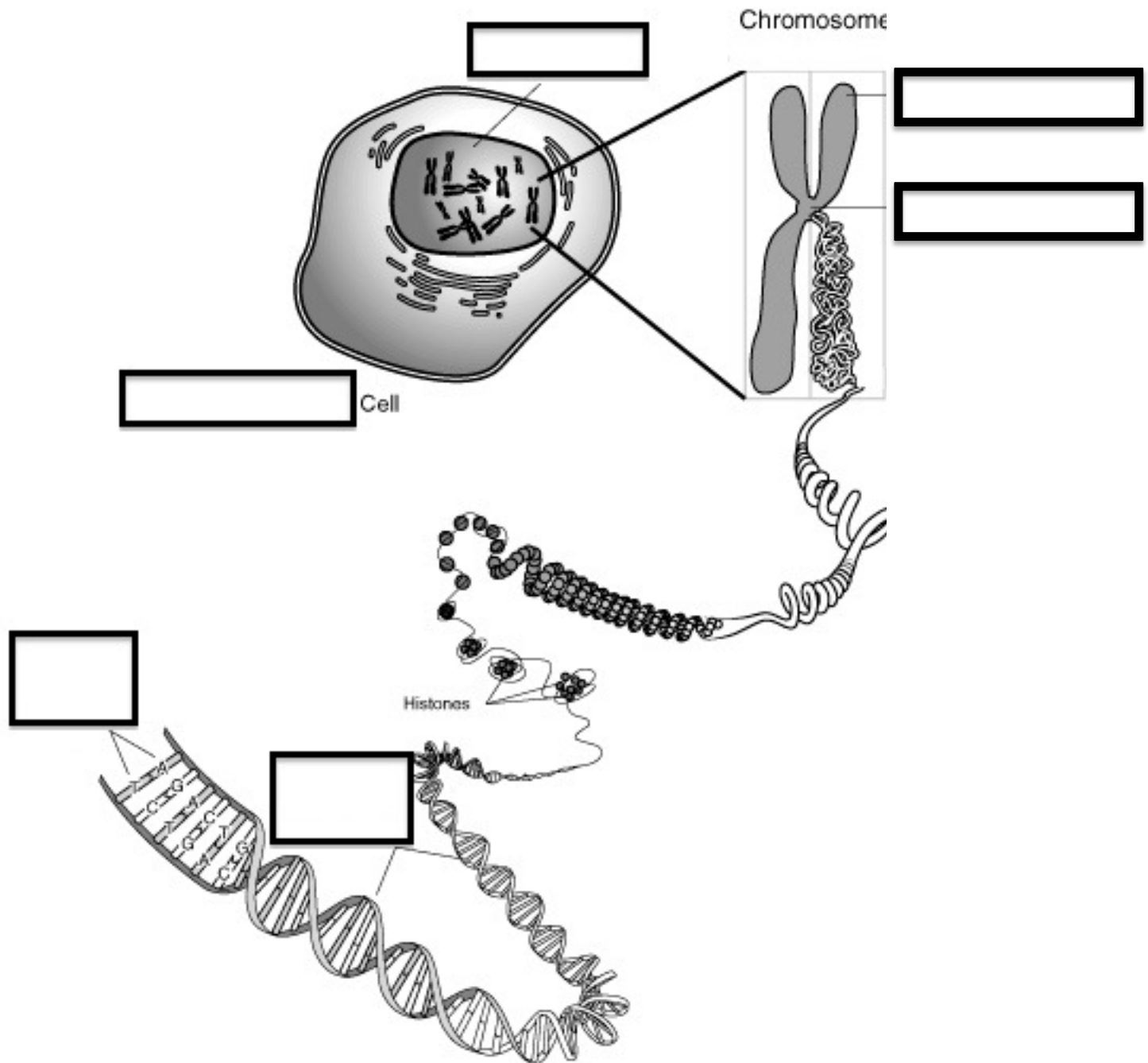
Date:

Using your notes and the word bank provided, complete the following diagram:

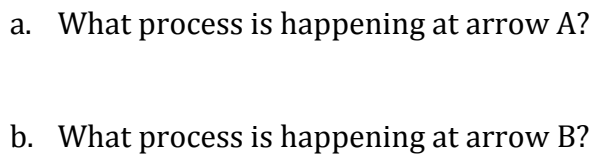
Sugar-Phosphate Backbone Nucleus

Centromere
Base Pairs

Eukaryotic
Sister Chromatid



1. What does it mean to say that two individuals are genetically identical?
2. If all of your cells came from pre-existing cells, describe why a muscle cell and nerve cell look different and have different functions.
3. Using the diagram on the front of this sheet, 1) circle the genetic material that is the most condensed and 2) put a star next to the genetic material that is the least condensed.
 - a. Why is it important for our DNA to condense?
4. The Central Dogma of biology is protein synthesis (show below). Complete the diagram:



TAC-CGG-AGT-TTG-GTA-TTC-ACA-ATT

- Methionine-alanine-serine-asparagine-glutamine-lysine-cysteine-stop
- Methionine-alanine-tyrosine-aspragine-histidine-lysine-cysteine-stop
- Methionine-alanine-serine-arginine-asparagine-histine-lysine-stop
- Methionine-alanine-serine-asparagine-histidine-lysine-cysteine-stop
- Methionine-alanine-tyrosine-asparagine-histidine-lysine-cysteine-stop

Name _____ Date _____

KWL Chart

Before you begin your research, list details in the first two columns. Fill in the last column after completing your research.

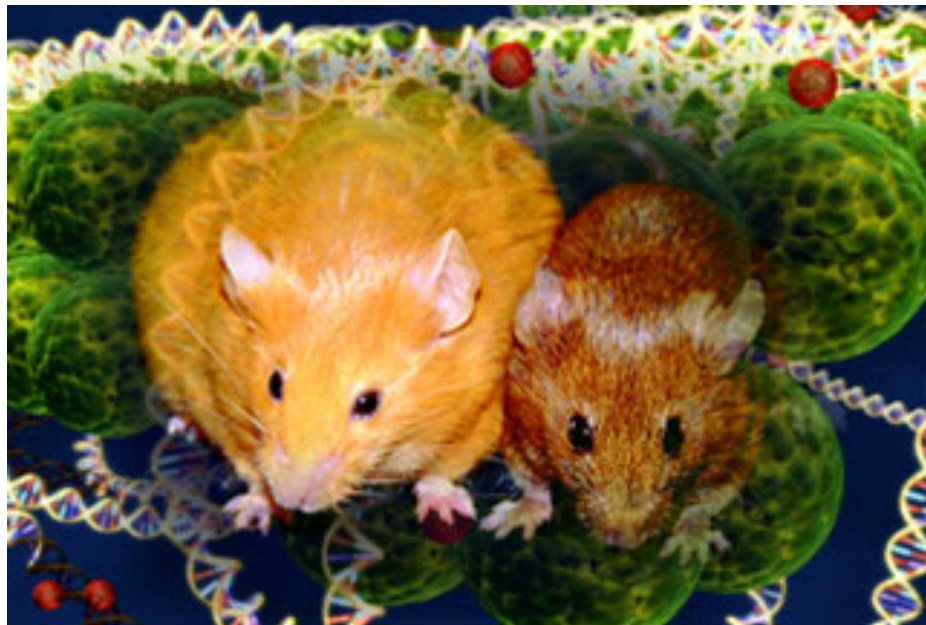
Topic _____		
What I Know	What I Want to Know	What I Learned



Epigenetics

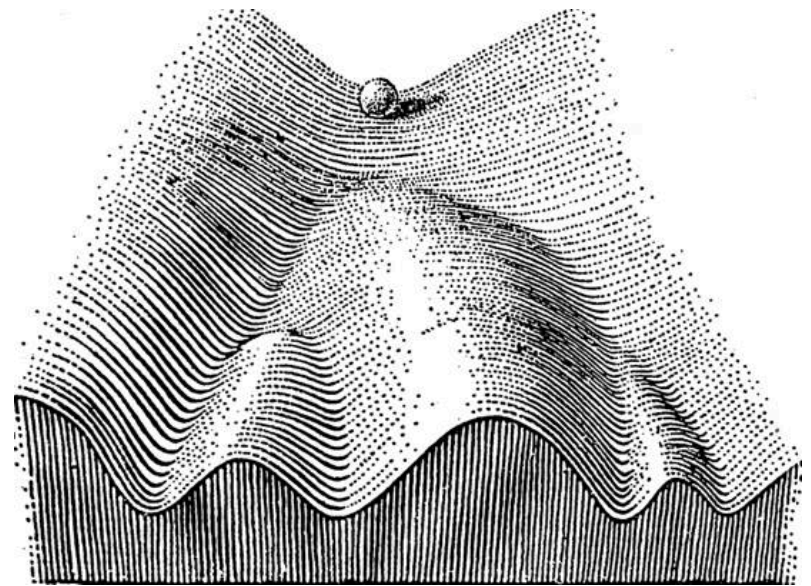
Discuss with a neighbor...

- + What does it mean to be “genetically identical?”
- + The two mice below are genetically identical. Why might they look different?



What is Epigenetics?

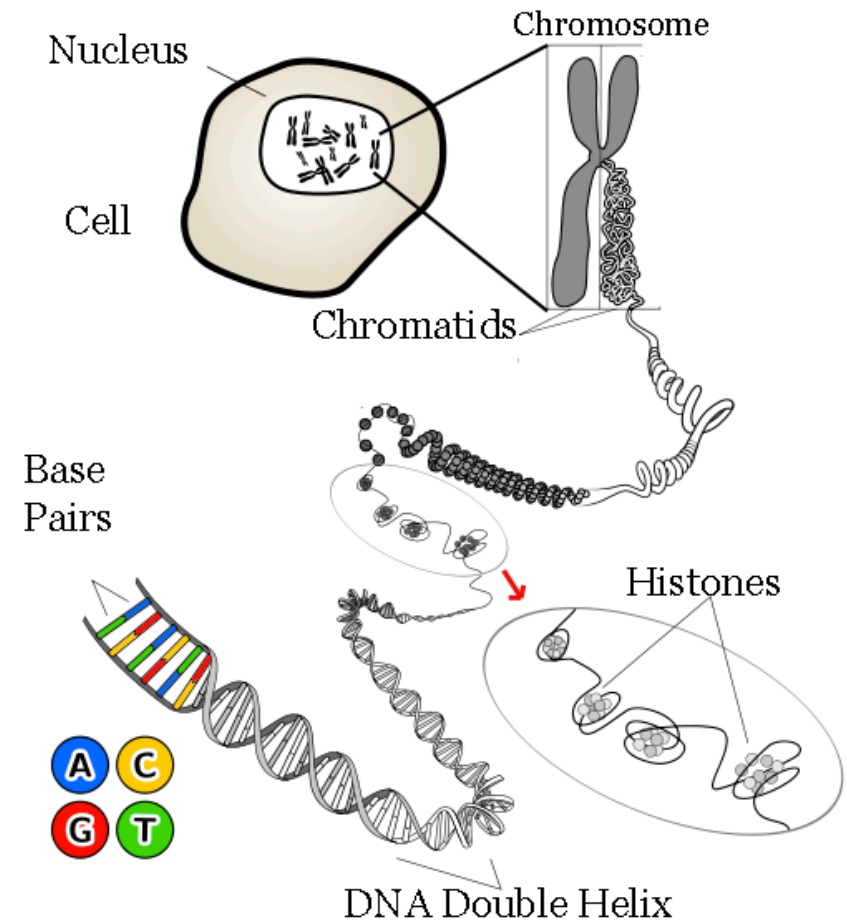
- + The study of environmental factors that turn genes on and off and affect how genes are “read”
- + Phenotypic variations that are not caused by changes in the DNA base sequence
- + Epigenetic changes affect cell fate



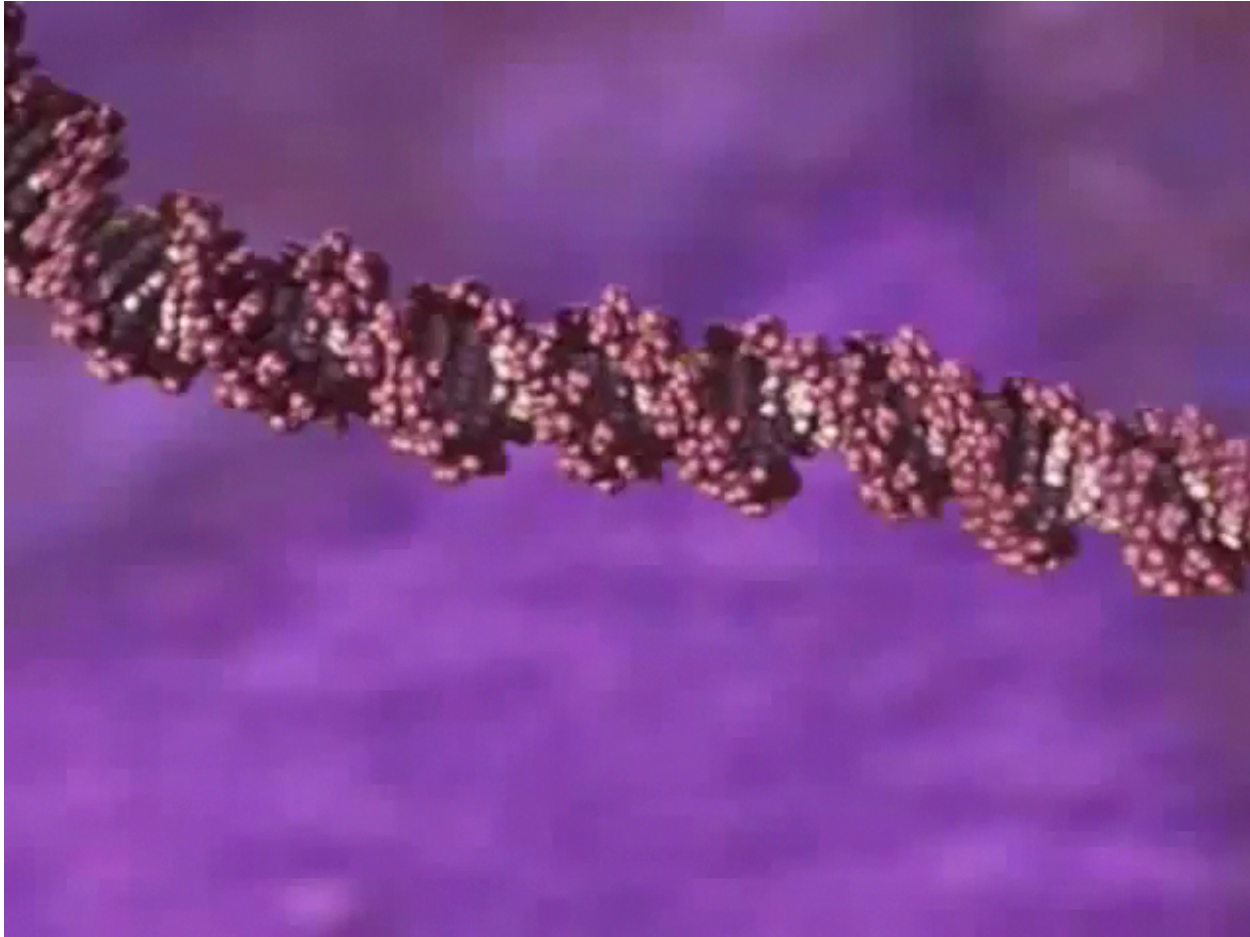
*Conrad Waddington's
Epigenetic Landscape*

Understanding Chromatin

- + Epigenetic modifications are largely the result of changes to chromatin
- + Chromatin = DNA + histone proteins
- + Access to DNA, from winding and unwinding chromatin, allows for gene expression
- + Transcription & Translation

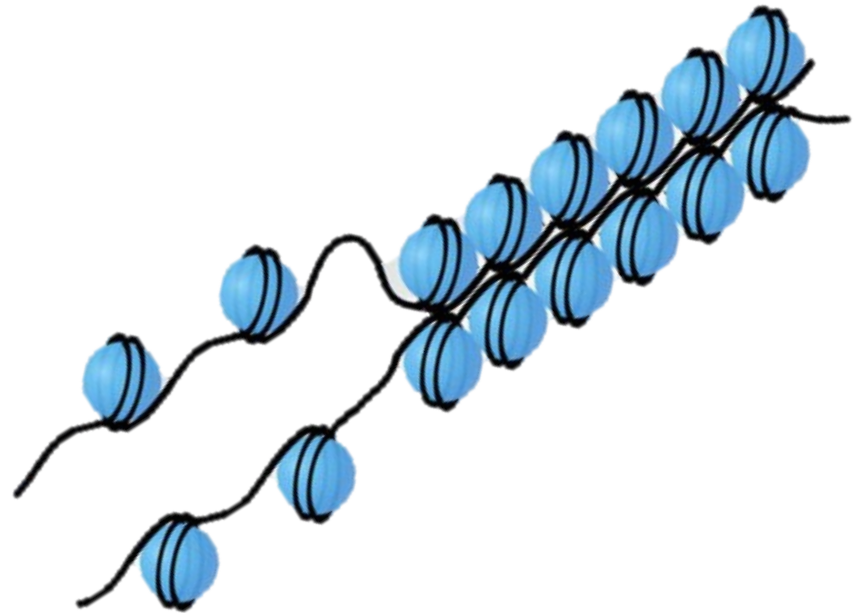


Understanding Chromatin



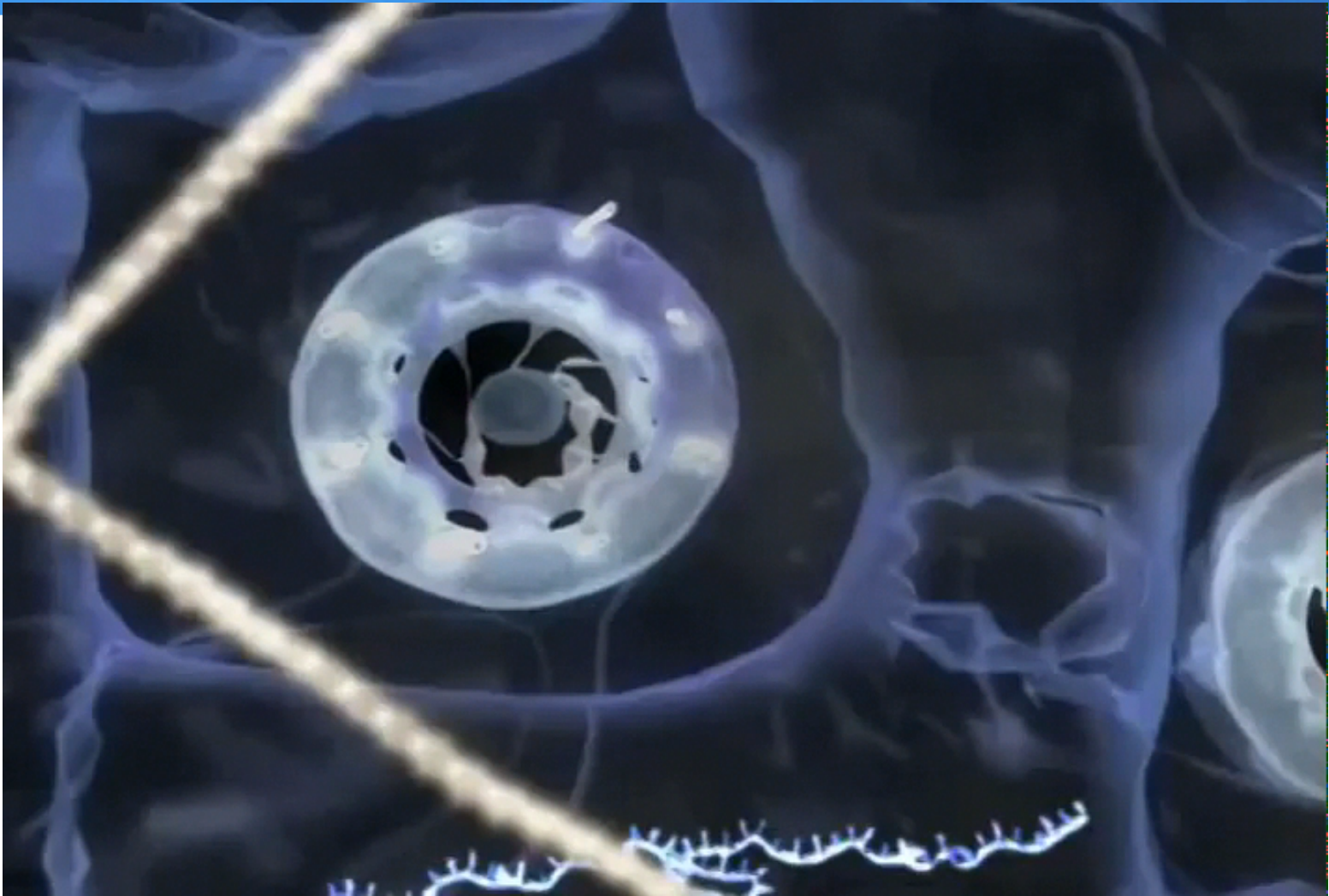
Histones

- + Protein subunits used to build nucleosomes
- + Look like “beads on a string”
- + May be modified to affect gene expression
 - + Loose winding = increased expression
 - + Tight winding = decreased expression

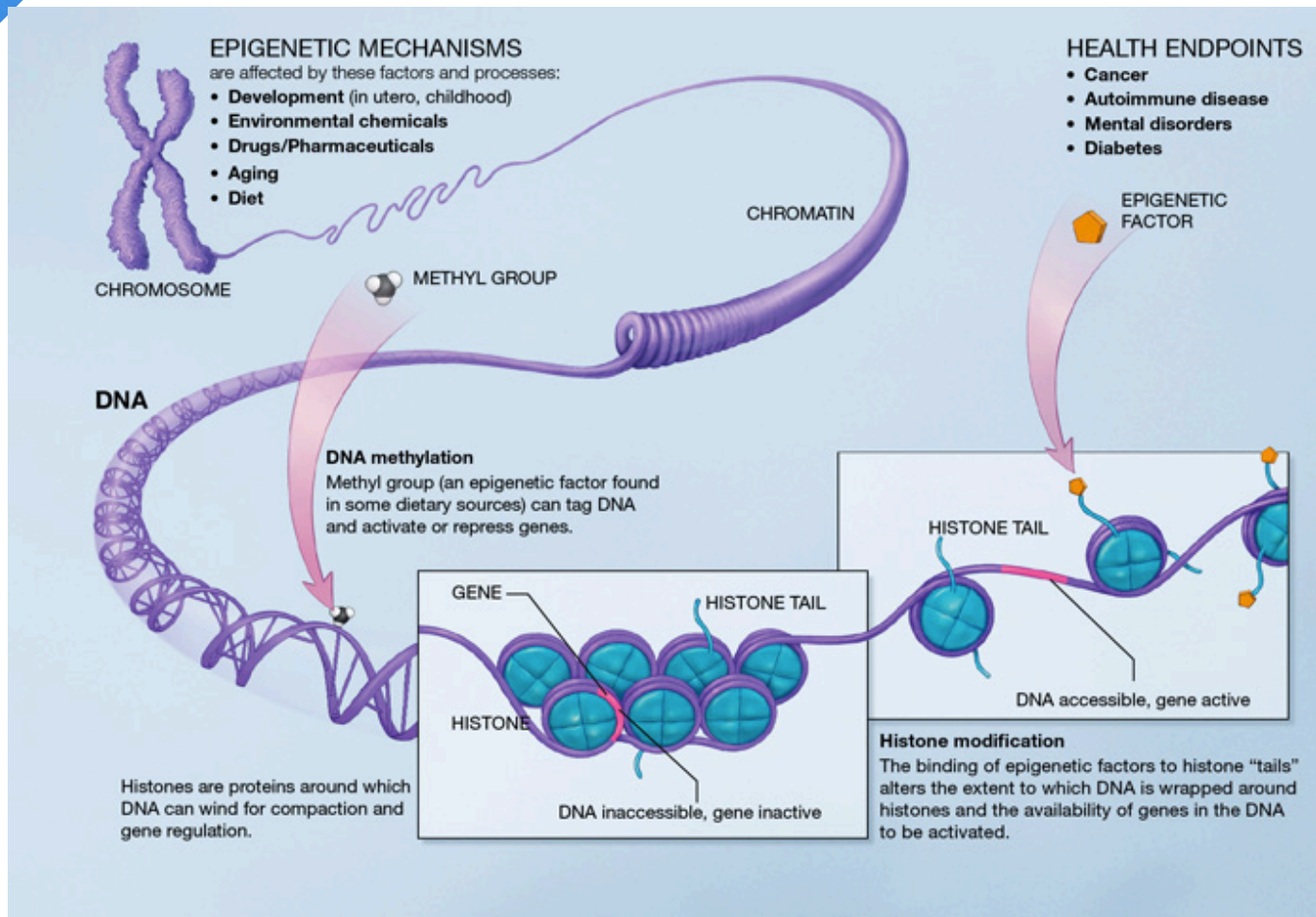


Adapted from en.wikipedia.org

Histones



Epigenetic Modifications



1. DNA Methylation
2. Histone Acetylation

1. DNA Methylation

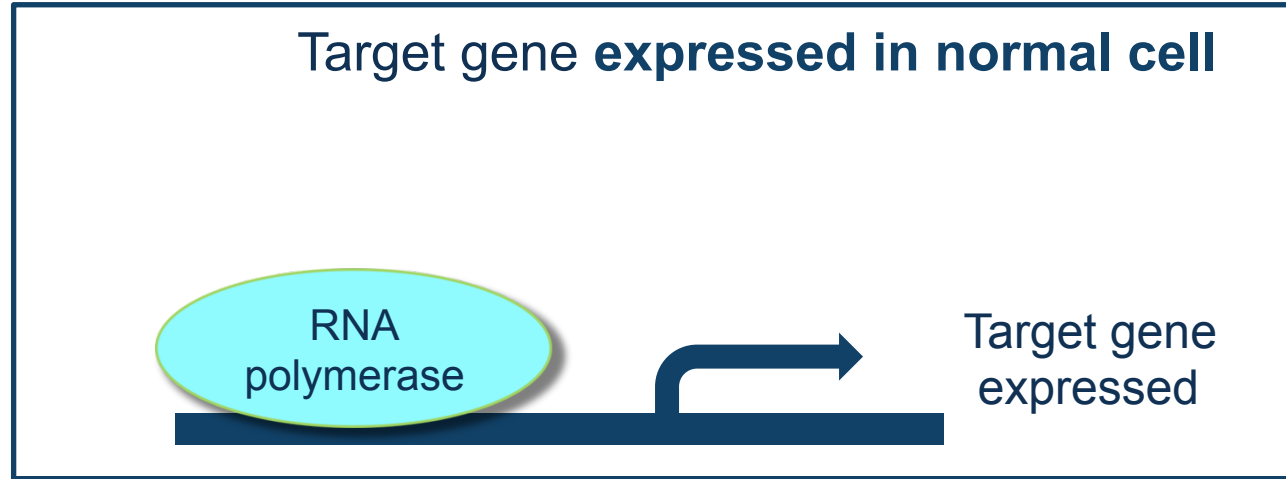
- + Addition of Methyl groups ($-\text{CH}_3$) to DNA prevents RNA Polymerase from binding
- + Prevents transcription (silences gene)
- + Protein not produced

Normal Protein Synthesis **DNA \rightarrow RNA \rightarrow Protein**

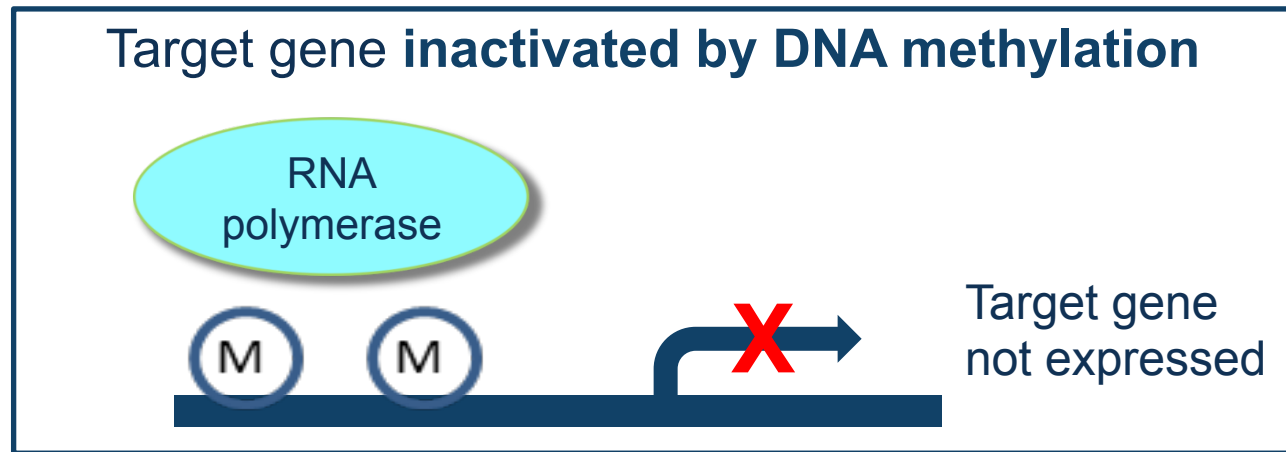
Protein Synthesis After Methylation **DNA \nrightarrow RNA \rightarrow Protein**

DNA Methylation leads to gene silencing

Normal
State



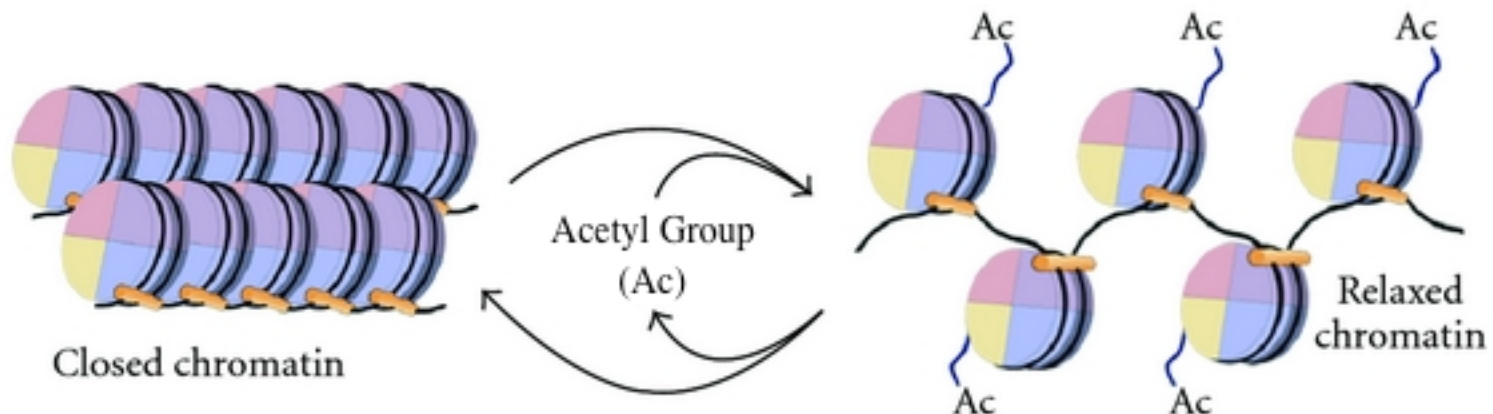
Epigenetic
Modification



Adapted from Dana Haine, UNC Superfund Research Program

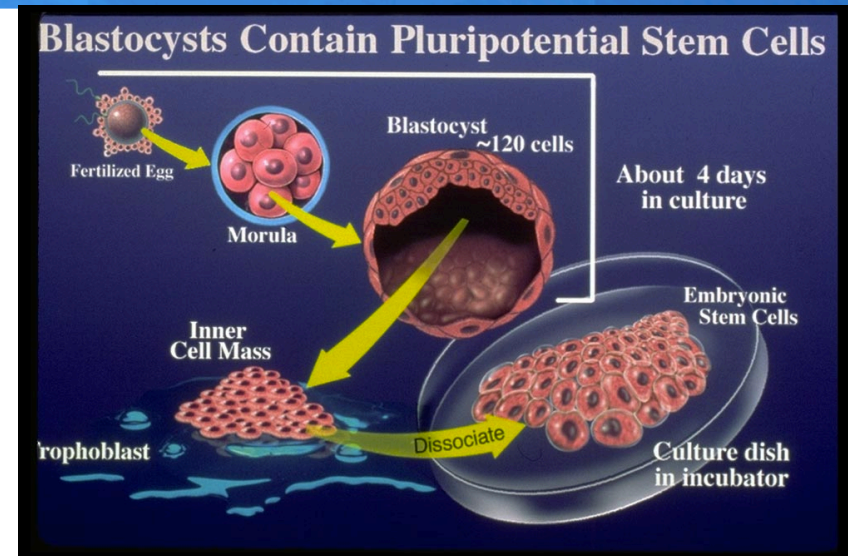
2. Histone Acetylation

- + Addition of Acetyl groups to histones loosens chromatin
- + If DNA is easily accessible, RNA Polymerase can bind
- + Rate of gene expression increases

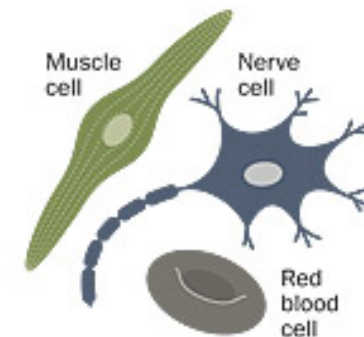


Epigenetics and Stem Cell Differentiation

- + Inner cells of the blastocyst act as pluripotent stem cells
- + Pluripotent Cells: Stem cells that can make every cell type in the body except placental cells
- + Totipotent Cells: Stem cells that have the potential to form every cell type in the body
- + Stem cells differentiate into new types of cells via methylation of genes that are not necessary for a particular cell type



EPIGENETIC MARKS DEFINE CELL TYPES



Famous Examples of Epigenetics

- + **Agouti Mice**

- + *pull audio from into to a tale of 2 mice

- + Show students interactive chapters

Famous Examples of Epigenetics

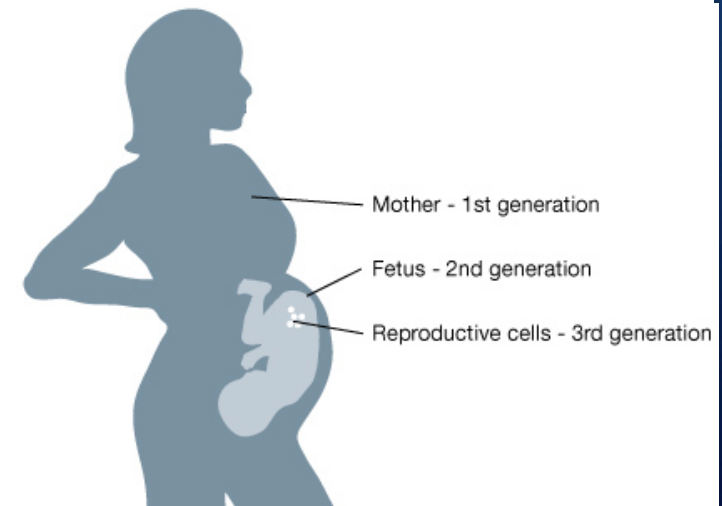
+ Dutch Hunger Winter

- + November 1944-Spring 1945
- + Entire group of people experienced famine at the same time (ideal study sample)
- + **Birth Weight** of children conceived during famine
 - + **Moms malnourished during 1st trimester** = babies born at normal weight; higher rates of obesity later in life
 - + **Moms malnourished during 3rd trimester** = babies born small; remained small; lower rates of obesity later in life



How is it Epigenetics?

- + 1st trimester is critical for development; 3rd trimester is critical for growth
- + Effects of malnutrition are more drastic during 1st trimester; body weight plays “catch up”
- + Some of these same traits now affect grandchildren who have not experienced famine, themselves
- + DNA did not change, but life histories of moms (and offspring) were altered in response to environment

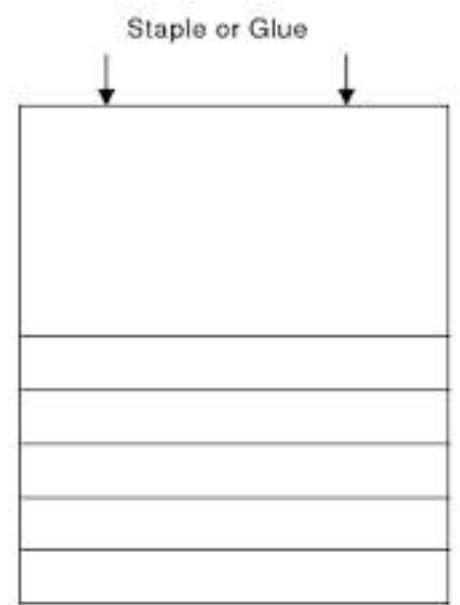


Epigenetics “Notes” Foldable

Name: _____

Instead of taking notes on Epigenetics, you will complete the following foldable, as the teacher presents the material.

1. Obtain 3 sheets of paper and stagger them in such a way so that 6 tabs are created.
2. Staple or glue the foldable together.
3. Label the tabs with the following titles from top (biggest tab) to bottom:
 - a. Epigenetics
 - b. What is it?
 - c. Chromatin & Histones
 - d. Epigenetic Modifications
 - e. Epigenetics and Cell Differentiation
 - f. Famous Examples
4. As the teacher presents the Power Point, be sure to write important information pertaining to each topic, on the appropriate tab.
 - a. You may also consider drawing any pictures that help you understand a particular concept.
 - b. **The order of the power point corresponds to the order of the tabs**
5. By the end of the presentation, you will not only have learned about epigenetics, but you will also have “notes” in a much more exciting format!
6. *Tips for taking “foldable notes”:*
 - a. *What is it? (be sure to define a concept)*
 - b. *Is there an easier way to explain it? (can you summarize or paraphrase the definition?)*
 - c. *What is the significance of the topic?*
 - d. *Is there a helpful diagram that you can draw?*
 - e. *Cool, interesting information*



Epigenetics

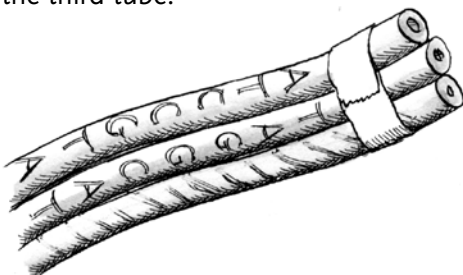
Epigenetics is a field of research that investigates heritable information carried in the cell that is not directly coded by DNA. The prefix *epi*, which comes from both Latin and Greek, means “above” or “outside.” The term epigenetics refers to mechanisms controlling gene expression that are independent of the DNA sequence itself.

Methyl groups are one kind of chemical known to have an epigenetic effect. Methyl groups occur

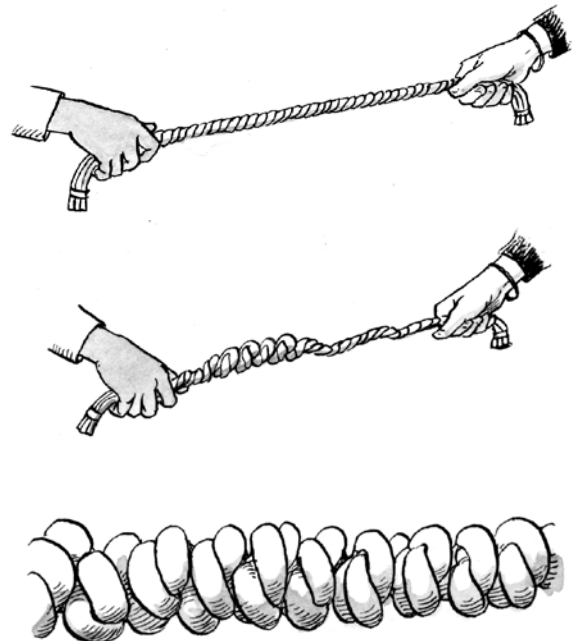
naturally, and the body obtains them through food and as natural products of metabolism. They enable the nucleus’s very tightly wound chromatin to uncoil. Since they originate outside the DNA, methyl groups are considered epigenetic factors. Today, you will build a model of chromatin and explore how chromatin can be chemically influenced by factors originating from “outside” the DNA.

Procedure

- 1 Build a model of chromatin. Gather the materials you need to make a model similar to the one your teacher demonstrated. Mark and assemble the three tubes as follows:
 - a Make the first “DNA” tube: Using a ballpoint pen, mark the length of the tube using combinations of the letters A, C, T, G. The letters should be large and in random order. You can use a letter more than once, and you can have two of the same letter in a row. These letters represent the amino acids of the nucleotides (A for Adenine, C for Cytosine, T for Thymine, and G for Guanine).
 - b Make the second “DNA” tube: Lay a second tube beside the first one. Where you’ve written an A on the first tube, mark a T on the second; where there’s a T on the first, write an A on the second. Similarly, where you’ve written a C on the first, mark a G on the second; where there’s a G on the first, mark a C on the second.
 - c Make the “histone” tube: Using a colored marker, put dots or stripes along the length of the third tube.



- d Hold the ends of the three tubes together, keeping them parallel (i.e., no twists, overlaps, or kinks). It does not matter which tube is next to which. Wrap tape around the ends, securing the tubes together. Repeat with the other end to make a single 24-inch, three-strand unit.
- 2 Twist the tubes. With one person holding each end of the triple bundle, begin twisting it into a spiral. When it begins to form knots, continue to twist slowly while pulling gently outward. Maintain tension so that the first spiral of knots forms into a secondary spiral of knots.



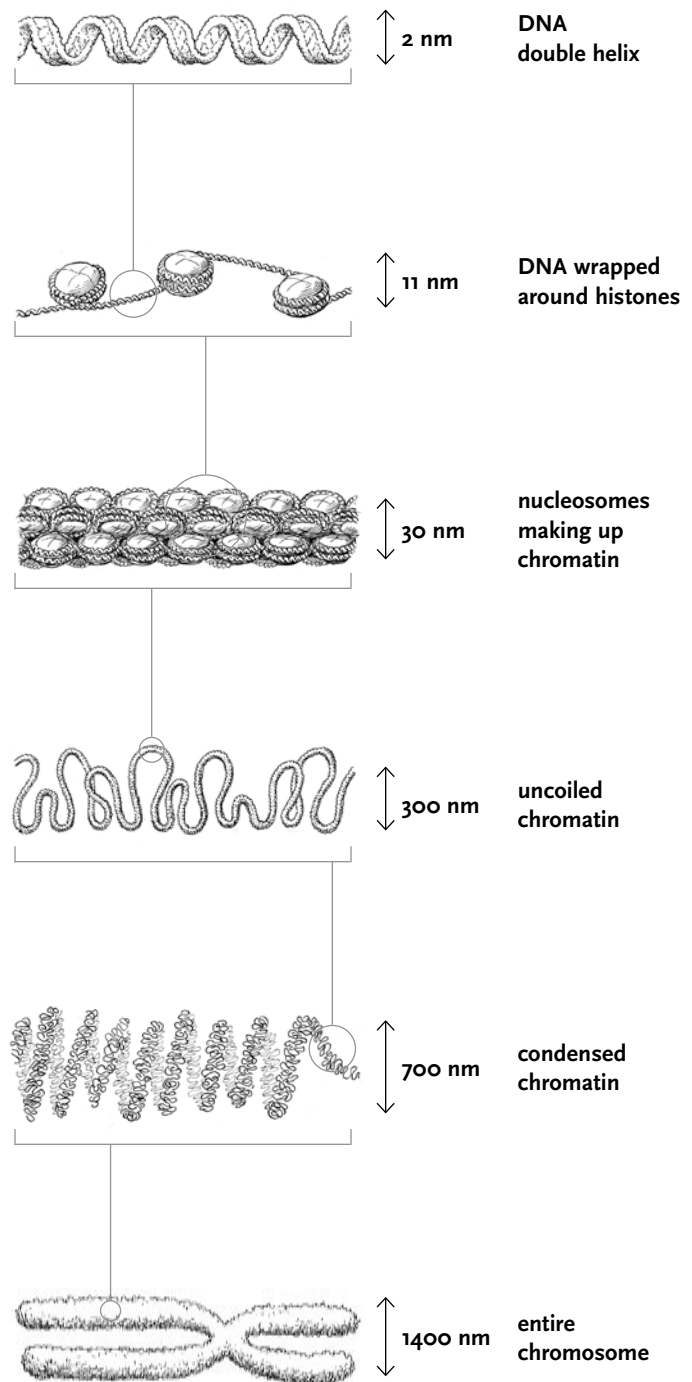
Epigenetics (cont.)

- 3 Show how epigenetic factors control the behavior of chromatin. Use your model to show how chromatin uncoils to reveal the sequence of the nucleotides so they can be “read” by enzymes and then transcribed by messenger RNA.
 - a Select a zone about six inches long near the middle of the twisted tubes. Mark this zone by attaching a binder clip to the “histone” tube at each end of the zone. The clips represent chemicals called methyl groups that are able to attach to the histone complex.
 - b Have a third person from your group work to carefully uncoil the three tubes in the six-inch zone marked off by the clips.
 - c Once this zone is uncoiled, read the sequence of base pair letters on the DNA tubes. This models the way that enzymes would “read” DNA base pairs to transcribe messenger RNA.
 - d After reading the base pair sequence, carefully recoil the three tubes and remove the clips.

Questions

Write your answers on a separate sheet of paper.

- 1 Why can it be difficult for enzymes to “read” DNA base pairs in a coiled nucleosome?
- 2 In your own words, explain the process of how methyl tags (represented by the binder clips) help chromatin uncoil to reveal the base pairs in a nucleosome.
- 3 How are methyl groups examples of an epigenetic factor?
- 4 What would happen if methyl groups stayed attached to the nucleosome forever and kept it continuously open?
- 5 List some ways that a nucleosome stuck in “continuous reading” mode might become unstuck.
- 6 List some strengths and weaknesses of this activity’s model of the DNA-chromatin complex.
7. Why might high-level exposures in early life to factors that lead to the accumulation of methyl groups have health consequences much later in life?



Strings of nucleosomes make up the chromatin. In the model, the secondary spiral of knots in the twisted tubing represents nucleosomes.



EPIGENETICS

DNA and Histone Model

ABSTRACT ↓

A 3-D cut-and-paste model depicting how histone, acetyl and methyl molecules control access to DNA and affect gene expression.

LEARNING OBJECTIVES ↓

- DNA is coiled around histones.
- Tightly coiled DNA is inaccessible to gene reading machinery.
- Methyl molecules bind to DNA and block access to genes.
- Acetyl molecules bind to histones and improve access to genes.

LOGISTICS ↓

TIME REQUIRED

- Class time: 50 min.
- Prep time: 15 min.

MATERIALS

- Copies of molecule cut outs and student directions
- Scissors
- Tape
- Paperclips

PRIOR KNOWLEDGE NEEDED

DNA, genes, cellular machinery “reads” genes and produces proteins

APPROPRIATE FOR

Primary Intermediate Secondary College



EPIGENETICS

DNA and Histone Model

CLASSROOM IMPLEMENTATION ↴

ACTIVITY INSTRUCTIONS

Distribute materials to pairs of students and instruct them to follow the directions on pages 1-4.

TIP: To save time, split the class in half. Ask student pairs in one half to complete the *Making DNA Inaccessible* portion of the activity (pages 1-2) and ask the other half to complete the *Making DNA Accessible* portion (pages 3-4). Have pairs of students share their different models with one another.

DISCUSSION POINTS

- Methyl and acetyl control gene expression by controlling access to DNA. Gene reading machinery in the cell is blocked by methyl that binds directly to DNA, or when DNA is wound tightly around histones. Access is easier when acetyl causes DNA to be wound more loosely around histones.
- Methyl and acetyl are epigenetic tags- chemicals that act as “switches” that determine gene expression without changing the underlying genetic code. Epigenetic tags turn genes on or off in response to cell signals, creating a dynamic layer of control called the epigenome.
- Enzymes play an important role in gene expression by facilitating the addition and removal of methyl and acetyl. In addition, enzymes are a part of the “Gene Reading Machinery”

OPTIONAL MODIFICATIONS

- Introduce the following vocabulary for more advanced students:
 - » Nucleosome: a single histone spool with its associated DNA. A sub-unit of chromatin.
 - » Chromatin: the material that makes up a chromosome.
 - » RNA Polymerase: the “gene reading machinery”
- Methyl attaches to DNA between a Cytosine (C) and Guanine (G) in locations known as CpG islands, where the frequency of C-G base pairs is higher than in other stretches of DNA. Instruct students to look for CpG islands along the DNA ribbon when attaching methyl molecules and place them accordingly. You may also use different colored paperclips in place of the methyl molecule cut outs to better highlight the area where methyl attaches to DNA.
- Choose a region of the DNA ribbon to represent a gene. Have students color it with a highlighter before attaching the DNA ribbon to their histone spools and winding. Ask students to visually keep track of the gene as they carry

QUANTITIES ↴

PER GROUP OF 2:

- One copy of directions and molecule cut outs, pgs. 1-8.
- Scissors
- Invisible tape
- 8 standard size paperclips (No. 1, approx. 3 cm long)



EPIGENETICS

DNA and Histone Model

out the activity. Discuss how methylation and acetylation would affect the expression of the gene.

- Because histone acetylation and DNA methylation are driven by constant cell signals, the physical structure of the genome is dynamic. Once they have constructed the model both ways (*Inaccessible DNA* and *Accessible DNA*), have students portray the dynamic nature of the genome's physical structure by having them manipulate their models in response to "gene on" or "gene off" signals. For example: Start with a constructed *Inaccessible DNA* model. At the prompt of "gene on" have students acetylate their histones, de-methylate and unwind their DNA ribbons. At the prompt of "gene off" have students de-acetylate their histones, wind their DNA ribbons more tightly and add methyl. Discuss when a cell might receive such signals.

EXTENSIONS

Make a chromosome!

- Pool together the DNA and Histone models from the whole class, plus others if possible, and stack them. The models you pool can be tightly wound and methylated, loosely wound and acetylated, or a combination of both. Be sure to connect the DNA ribbons to form one long, continuous strand.
- Students will see that chromosomes are made of DNA and histones.

ACKNOWLEDGEMENTS ↴

This activity is a product of the 2008 Beyond the Central Dogma Master Teacher Summer Institute.

Funding was provided by a Science Education Partnership Award from the National Center for Research Resources, a component of the National Institutes of Health.



PERMISSIONS ↴

Please see: <http://learn.genetics.utah.edu/permissions/> to read our Permissions Policy.

NAME _____

DATE _____

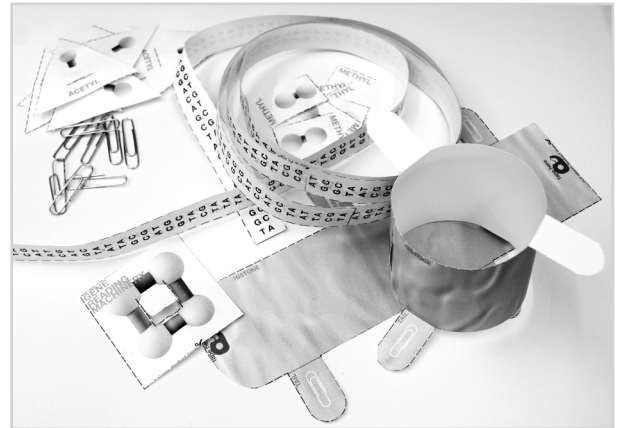


DNA and Histone Model

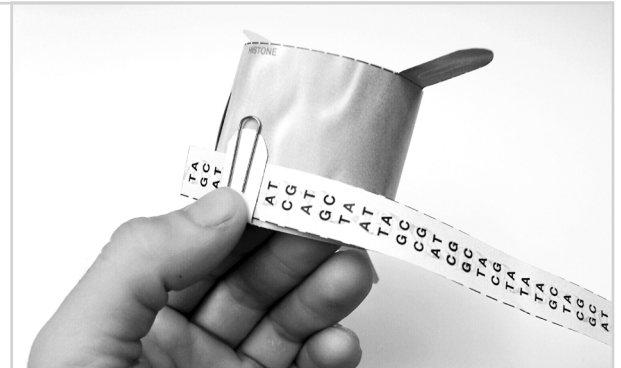
How do molecules control gene expression?

MAKING DNA **INACCESSIBLE**

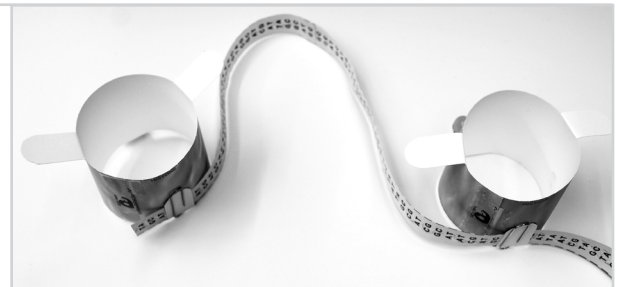
Cut out all of the molecules on pages 5-8, assemble the DNA ribbon and histone spools. Gather 8 paperclips.



In the cell, DNA is wound around spool-like molecules called histones. Attach one end of the DNA ribbon to a histone. Fold one of the histone tails over the DNA ribbon to help hold it in place. Secure it with a paperclip.



Attach the remaining histones along the DNA ribbon at a distance of 2 strips of DNA apart (roughly 16 cm).



Hold the first histone upright in one hand. Wind the DNA ribbon clockwise around it roughly two times or until you bump in to the next histone. Fold all of the histone tails over the DNA ribbon to help hold it in place and secure with a paperclip.

In a real cell, a length of DNA wraps around a histone roughly 1.7 times and histone tails wrap around the wound DNA similarly.



NAME _____

DATE _____



DNA and Histone Model

MAKING DNA INACCESSIBLE cont.

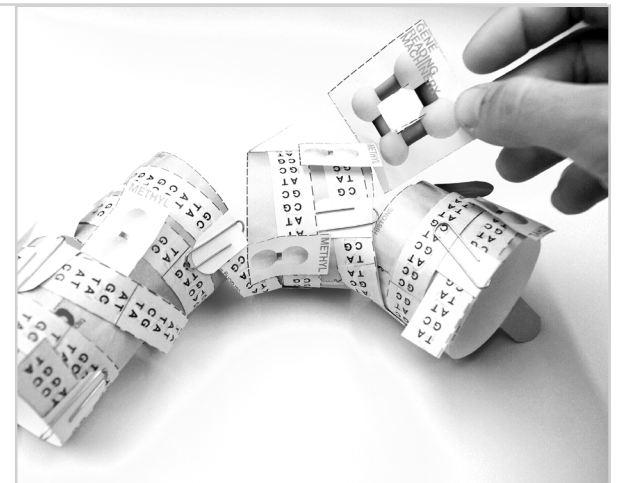
Trying not to fold or bend the DNA ribbon, wind it around the next histone. Again, fold the histone tails around the DNA ribbon and secure with a paperclip. Repeat until all of the DNA ribbon has been wound. The histones should begin to stack on top of one another as you wind.



When DNA is wound tightly around histones, there tends to be a lot of methyl molecules bound to it. The methyl molecules cover the DNA, making it unreadable to gene reading machinery. Use tape to attach the methyl molecule cut outs to exposed areas of your DNA ribbon.



Genes become active when gene reading molecules attach and move down a length of accessible DNA, "reading" the DNA code as they go along. Try to attach and move the Gene Reading Machinery cut-out to any length of the DNA ribbon that is not spooled around a histone or covered by methyl. Can the machinery read any significant stretch of DNA? Would this be an active, or inactive gene?



Remove the methyl molecules and de-construct your model if moving to the next step: MAKING DNA ACCESSIBLE

NAME _____

DATE _____

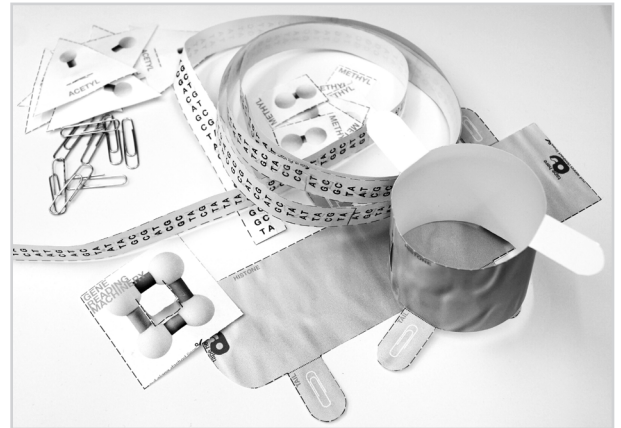


DNA and Histone Model

How do molecules control gene expression?

MAKING DNA **ACCESSIBLE**

Cut out all of the molecules on pages 5-8, assemble the DNA ribbon and histone spools. Gather 8 paperclips.



DNA is wound around spool-like molecules called histones. At times, acetyl molecules bind to histone tails. Attach two acetyl molecules to each histone at different locations. To attach the molecules, pull a histone tail through the cut in the center of the acetyl molecules. Now your histones are “acetylated”.



Attach an acetylated histone to one end of your DNA ribbon, secure it with a paperclip.

Attach the remaining acetylated histones along the length of the DNA ribbon at distances of 2 DNA strips apart (roughly 16 cm).



Hold the first histone upright in one hand. Wind the DNA ribbon clockwise around it two times or until the first histone touches the next one.



NAME _____

DATE _____



DNA and Histone Model

MAKING DNA ACCESSIBLE cont.

In a real cell, the addition of acetyl molecules cause the histones to distance themselves from one another. Be sure that no part of the neighboring histones, including the acetyl molecules are touching. If they are, unwind the DNA ribbon a little bit to put some space between the histones. Secure the DNA ribbon with a paperclip.



Wind the DNA ribbon clockwise around the next histone. Again, be sure that no part of neighboring histones are touching then secure the DNA ribbon with a paperclip. Repeat until the DNA ribbon has been wound around all the histones. The histones and DNA should be spooled loosely, with some space between histones.



Genes become active when gene reading molecules attach and move down a length of accesible DNA, "reading" the DNA code as they go along. Try to attach and move the Gene Reading Machinery cut-out to any length of the DNA ribbon that is not spooled around a histone. Can the machinery read any significant stretch of DNA? Would this be an active, or inactive gene?



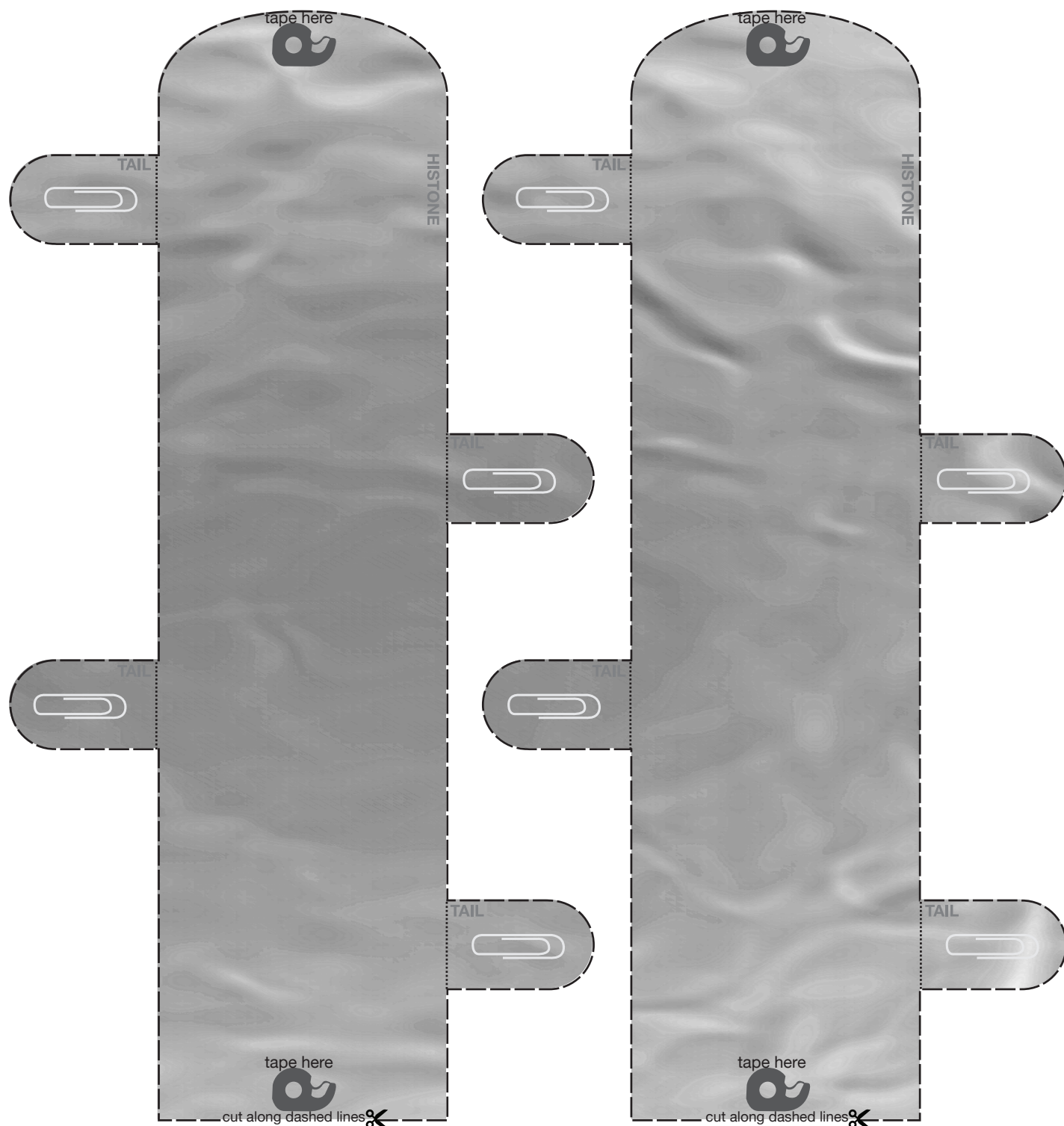
NAME _____

DATE _____



HISTONE SPOOLS - Set 1

Tape the ends of each histone together to form spools.



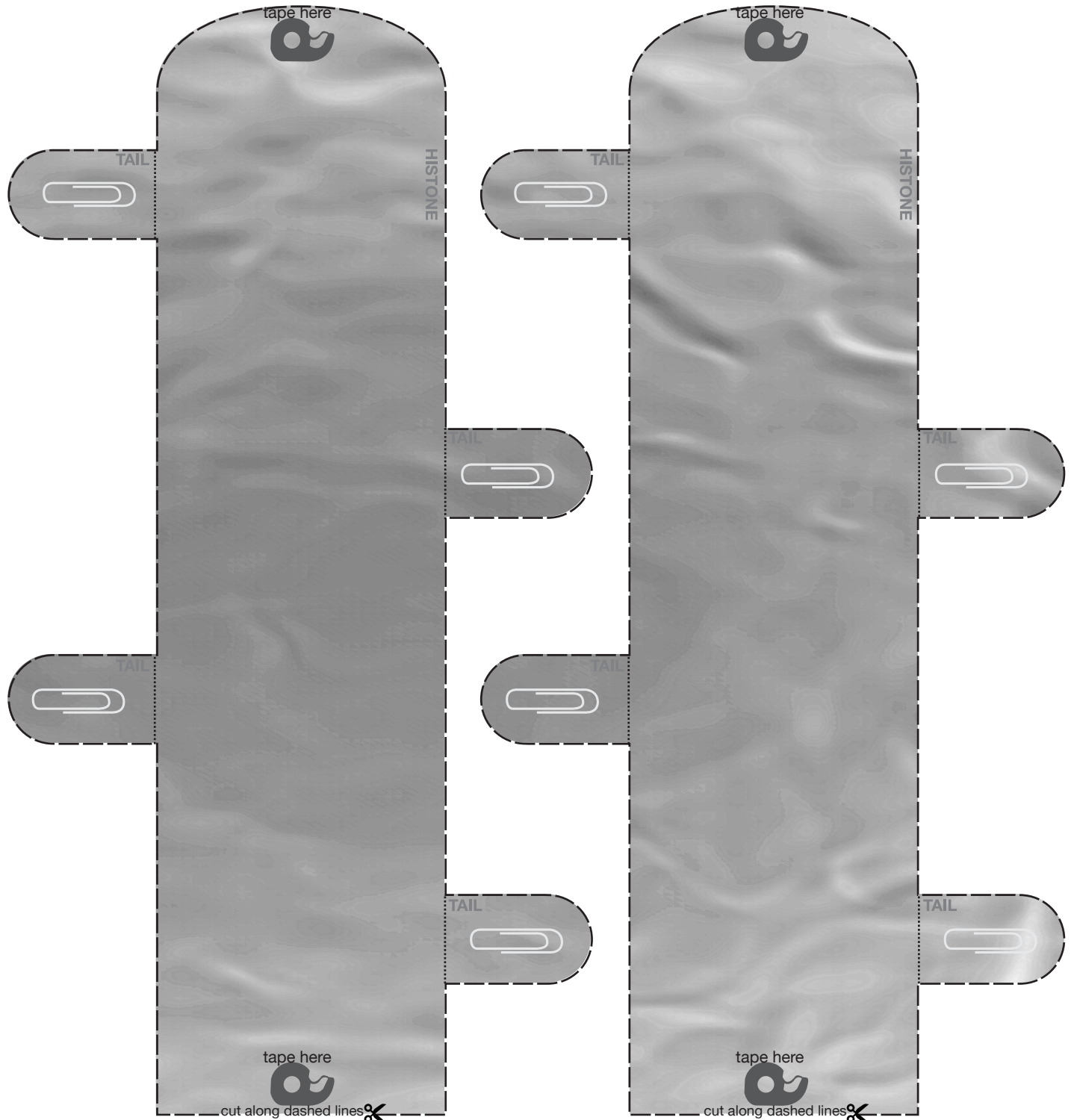
NAME _____

DATE _____



HISTONE SPOOLS - Set 2

Tape the ends of each histone together to form spools.



NAME _____

DATE _____

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<http://Teach.Genetics.utah.edu>



DNA Strips

Tape the short ends of the DNA strips together to form one long DNA ribbon.

TA	TA	CG	GC	CG	CG	TA	GC
GC	GC	AT	TA	AT	TA	AT	TA
GC	AT	GC	GC	GC	GC	AT	CG
AT	TA	TA	GC	GC	TA	CG	AT
GC	CG	AT	CG	TA	GC	GC	TA
AT	AT	CG	AT	AT	TA	AT	AT
CG	AT	GC	GC	CG	AT	GC	CG
AT	CG	CG	GC	GC	GC	CG	TA
TA	AT	AT	AT	AT	AT	AT	GC
TA	GC	AT	TA	GC	TA	GC	TA
GC	TA	CG	TA	CG	TA	CG	GC
AT	AT	GC	AT	AT	AT	TA	CG
TA	TA	AT	TA	CG	TA	GC	GC
CG	GC	CG	AT	CG	AT	TA	CG
CG	CG	AT	TA	GC	TA	CG	GC
GC	AT	TA	AT	AT	GC	GC	TA
TA	CG	AT	CG	TA	TA	AT	AT
CG	GC	TA	GC	TA	CG	TA	TA
TA	TA	TA	AT	AT	GC	TA	CG
TA	CG	CG	CG	TA	AT	AT	GC
GC	TA	TA	TA	AT	CG	GC	CG
TA	TA	TA	GC	TA	AT	CG	TA
AT	TA	TA	TA	AT	GC	TA	TA
TA	GC	GC	CG	TA	CG	AT	AT
GC	TA	CG	GC	CG	TA	CG	TA
CG	CG	AT	CG	TA	AT	GC	AT
AT	GC	GC	AT	GC	CG	TA	AT
CG	AT	GC	CG	TA	GC	AT	GC
GC	CG	AT	AT	GC	AT	TA	CG
AT	AT	GC	GC	GC	GC	AT	AT
AT	TA	TA	TA	CG	CG	TA	GC
CG	GC	GC	AT	TA	AT	GC	CG
AT	GC	TA	TA	GC	GC	TA	GC
GC	AT	GC	CG	TA	GC	CG	AT
TA	GC	TA	TA	CG	TA	CG	TA

- cut along lines ✂

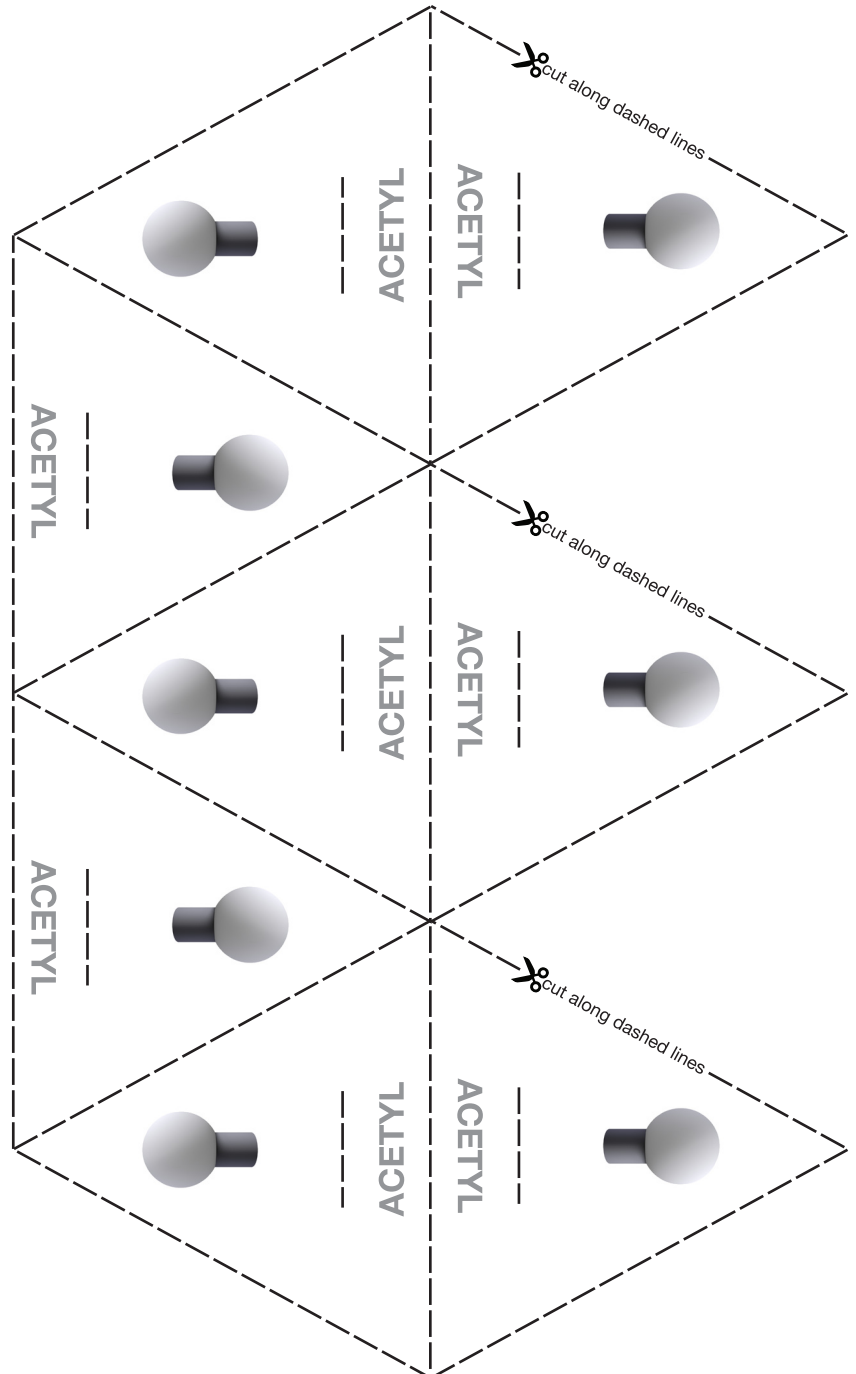
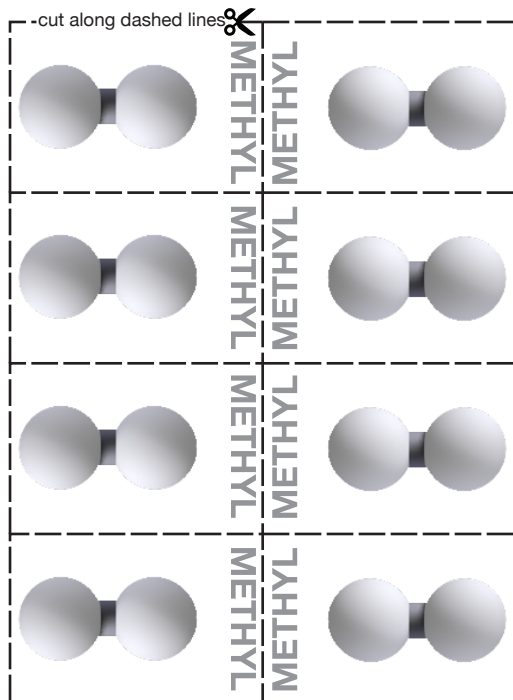
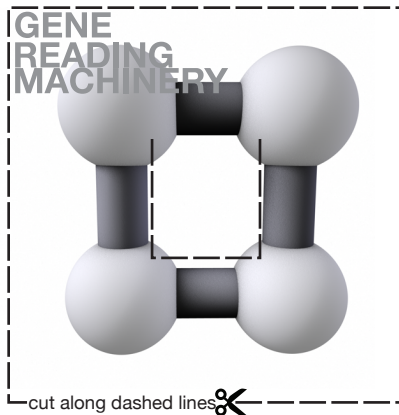
NAME _____

DATE _____



Methyl, Acetyl and Gene Reading Machinery

Cut out and slit along interior dashed lines.



Community Engagement Assessment

Name:



What better way to demonstrate mastery of epigenetics than teach it to other people?! Instead of a test for this unit, you will be completing an assignment worth **2 project grades!**

Essentially, you will be explaining the concept of epigenetics to a group of at least 3 people (who are not your biology classmates) with at least a middle school education. This group of people can be students in another class or school, friends and family at your church or community center, or any other public forum.

Project Grade #1:

To help support your community engagement presentation, you will develop an education video, module, tutorial, or classroom lesson. You should not simply lecture for your presentation. Within your video, tutorial, etc., you will provide audience members with:

- 1. An overview of epigenetics**
- 2. A comparison of the genome and epigenome (think about your infographic)**
- 3. A spotlight on a particular epigenetic concept or case study that is relevant and valuable for community members**
 - *It may serve the community best to discuss an epigenetic concept with implications for human health*
 - *You may draw upon the In-Class Inquiry research done by your peers*

There are a variety of ways to convey this information to your audience. The presentation that you give may simply be informative, or be framed as a persuasive argument. I would encourage you to interact with your audience members as much as possible. You may choose to use one or more of the following tools provided below, or develop your own project proposal (make sure you get my approval).

- [PowToon](#): Create an animated film to present and explain your topic. This could serve as your entire project or supplement your presentation.
- [Aurasma](#): Using the Aurasma application, guide audience members through an interactive module where they can watch videos, complete surveys, and engage with your topic.
- [YouTube](#): Create a YouTube tutorial to guide viewers through your topic. See videos from [Khan Academy](#), [Bozeman Science](#), and [SciShow](#) for inspiration.
- [Prezi](#): Using videos and animation, provide your viewer with a unique way to experience your presentation.

Project Grade #2: Prove that you presented your project!

- Invite me (or another teacher) to attend your presentation
- Ask audience members to complete a survey, evaluating your presentation and their understanding of the topic
- Film or take pictures during your presentation

PROJECT GRADE #1

Category	4 points	3 points	2 points	1 point
Overview of Epigenetics	Presentation materials provide an in-depth explanation of epigenetics with elaborate details. Audience is well informed.	Presentation materials sufficiently cover the topic of epigenetics and provide the audience with a good understanding.	Presentation materials somewhat discuss the topic of epigenetics, but does not cover all relevant details. Audience is left with questions.	Presentation materials do not adequately cover the topic of epigenetics. Audience members walk away confused.
Comparison of Genome & Epigenome	A thorough review of similarities and differences is provided. Specific examples are provided.	Terms are compared and contrasted thoroughly, but examples are too general.	The presentation only addresses similarities or differences (not both). Examples distract from the main idea.	Many details are not included or appear in an illogical order. Poor understanding of the terminology.
Epigenetic Spotlight	Presents a thorough analysis of the identified case. Makes appropriate and meaningful connections between spotlight topic and course content (epigenetics).	Presents a mostly thorough analysis of the identified case. Makes appropriate connections between spotlight topic and course content.	Presents a vague, somewhat disconnected analysis of the case study. Struggles to connect the case study to the course content.	Presents an incomplete analysis of the spotlight topic. Makes little to no connection to course content.
Use of Presentation Technology	Greatly enhances content and purpose.	Supports content and purpose.	Does not distract audience from content and purpose.	Distracts audience from content and purpose.
Organization	Extremely well planned and has smooth transitions.	Well planned and follows a logical sequence.	Some evidence of planning, but not always logical.	No evidence of planning or organization.
			Total: _____/20 points	

PROJECT GRADE #2: Proof of Presentation (20 points): ☐ yes ☐ no

Notes/Feedback: