Epigenetics; Monozygotic Twin Studies

University of Florida Center for Precollegiate Education and Training

EPIGENTICS; MONOZYGOTIC TWIN STUDIES

UF | Center for Precollegiate Education and Training
UNIVERSITY of FLORIDA

Author: Renae Allen

This curriculum was developed as part of *Biomedical Explorations: Bench to Bedside*, which is supported by the Office Of The Director, National Institutes Of Health of the National Institutes of Health under Award Number R25 OD016551. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Center for Precollegiate Education and Training

PO Box 112010 • Yon Hall, Room 331

Gainesville, FL 32611

Phone 352.392-2310• Fax 352.392-2311

This curriculum was developed in the laboratory of:

Jorg Bungert, PhD
Associate Professor
Department of Biochemistry and Molecular Biology
College of Medicine

The focus of our laboratory is to analyze mechanisms regulating gene expression during erythroid cell differentiation. The beta-globin genes are regulated by a locus control region (LCR). The LCR is composed of several DNase I hypersensitive (HS) sites that together mediate chromatin structure alterations and high-level transcription throughout erythroid development. The human beta-globin gene locus consists of five genes that are expressed in a developmental stage specific manner in erythroid cells. During development the different proteins encoded by the beta-globin gene locus (ε, Aγ, Gγ, δ, and βglobin) dimerize with a-globin subunits to form hemoglobin. The beta-type globin genes are expressed at extremely high levels in erythroid cells which is mediated by the LCR.

Results from our previous work suggest that the individual LCR HS elements interact to generate a higher order structure, referred to as the LCR holocomplex, and that this complex communicates in a stage-specific manner with individual globin genes. We also found that the LCR recruits transcription complexes and proposed that the LCR serves as the primary site of transcription complex recruitment and assembly in the beta-globin gene locus. We use transgenic mice and cell culture to identify and functionally characterize cis-regulatory DNA elements and trans-acting components involved in the regulation of the beta-globin genes. We utilize artificial DNA binding domains to modulate and characterize the function of transcription factor binding sites in the beta-globin gene locus. We also use a variety of molecular techniques, including chromatin immunoprecipitation (ChIP), ChIP-sequencing, shRNA mediated knockdown, and overexpression of dominant negative transcription factors to analyze transcription factor function and globin gene regulation.

TABLE OF CONTENTS

AUTHOR'S NOTE

I became a high school science instructor in 1985 with a major in Geology and minor in Biology. The school district where I have been continuously employed is one of the smallest in the state, therefore, if a variety of science curriculum was to be offered to students I would have many lesson preparations to make. Throughout the 1980s and 1990s, I taught Biology, Earth and Space Science, Anatomy and Physiology, Physics, Physical Science, Marine Science and occasionally Chemistry at both the general and honors levels. Teaching a great variety of courses proved beneficial when the Excellent Teaching Program was adopted which implemented the National Board Certified Teacher Exams as the measure of qualification. The Adolescent and Young Adult Science certification required teachers to produce portfolios, videos of teaching practice, and pass subject area testing which included knowledge of Earth and Space Science, Biology, Chemistry and Physics. Science teachers found it difficult to qualify because most are certified in a specific subject area and are not necessarily knowledgeable in all areas of science. My teaching experience using a variety of science curriculum led to success in being among the first nationally certified teachers in the state. Today, I have the privilege to teach Chemistry and Advanced Placement classes in Environmental Science and Biology, offering college credit potential to high school students. I have enjoyed the experience of being part of a system of constantly changing science curriculum and content focus.

When I began teaching, the technique of DNA analysis was in its infancy. Large quantities of DNA were required for testing. Application for forensic purposes or other forms of identification were not reliable. Biology textbooks included content on the characteristics of life, basic chemistry concepts, introductory cell science with reference to mitosis and meiosis, bacteria, protists, fungi, plants, animals and humans with reference to natural selection and evolution and at least one chapter on Mendelian genetics. Today, the concept emphasis of a high school biology class has completely changed. Molecular biology, gene expression, and biotechnology were not only missing in a 1980s textbook but are now seen as topics of critical importance in biology curriculum. Thirty years later, the concept of ***epigenetic inheritance*** is usually relinquished to a paragraph in high school biology textbooks. However, in the future, this topic will grow to become one of critical importance while the transition in biology content for high school students will include concepts we can only imagine today.

INTRODUCTION

Epigenetic inheritance provides an opportunity for students to revisit the transcription process in a manner that will reinforce understanding of the central dogma of molecular biology. Epigenetics as a theme of study incorporates concepts of molecular biology, gene expression, biochemistry, and implications for treatment of diseases or disorders that affect health and behavior.

In addition to transcription factors, students will be captivated by the idea that environmental exposures or stress may turn genes "on" or "off". Using monozygotic twins as examples, students can easily comprehend how individuals with the same original genome diverge over time due to epigenetic influences. Creating interview questions to assess differences in monozygotic twins of different ages as a class activity will engage students to contemplate possible phenotypic changes produced by epigenetic changes in the twins.

Students will gain background knowledge through an interactive lecture that reviews transcription and includes the DNA methylation mechanism for epigenetic change. Background knowledge will be reinforced through video and slide presentations with assessments. A reading assignment using monozygotic twins for reference will also serve to reinforce content as well as provide an interesting example students will understand.

The lesson will conclude with a laboratory activity; *Detecting Epigenetic DNA Methylation in Arabidopsis.* This activity utilizes methylation-sensitive enzymes to explore epigenetics and gene expression that affects flowering in Arabidopsis plants. Students gain experience with DNA extraction, restriction enzyme digest, PCR, gel electrophoresis and bioinformatics.

TIPS ABOUT THIS CURRICULUM

Lesson Plan Format: All lessons in this curriculum unit are formatted in the same manner. In each lesson you will find the following components:

KEY QUESTION(S): Identifies key questions the lesson will explore.

OVERALL TIME ESTIMATE: Indicates total amount of time needed for the lesson, including advanced preparation.

LEARNING STYLES: Visual, auditory, and/or kinesthetic.

VOCABULARY: Lists key vocabulary terms used and defined in the lesson. Also collected in master vocabulary list.

LESSON SUMMARY: Summary of what the lesson will cover and how this content will be covered. Also collected in one list.

STUDENT LEARNING OBJECTIVES: Focuses on what students will know, feel, or be able to do at the conclusion of the lesson.

STANDARDS: Specific state benchmarks addressed in the lesson. Also collected in one list.

MATERIALS: Items needed to complete the lesson. Number required for different types of grouping formats (Per class, Per group of 3-4 students, Per pair, Per student) is also indicated.

BACKGROUND INFORMATION: Provides accurate, up-to-date information from reliable sources about the lesson topic.

ADVANCE PREPARATION: This section explains what needs to be done to get ready for the lesson.

PROCEDURE WITH TIME ESTIMATES: The procedure details the steps of implementation with suggested time estimates. The times will likely vary depending on the class.

ASSESSMENT SUGGESTIONS: Formative assessment suggestions have been given. Teachers should feel free to create additional formative and summative assessment pieces.

EXTENSIONS: (ACTIVITIES/LITERATURE) There are activities and reading sources available to augment and enhance the curriculum. They have been included.

RESOURCES/REFERENCES: This curriculum is based heavily on primary sources. As resources and references have been used in a lesson, their complete citation is included as well as a web link if available. All references and resources are also collected in one list.

STUDENT PAGES: Worksheets and handouts to be copied and distributed to the students.

TEACHER MASTERS: Versions of the student pages with answers or the activity materials for preparation.

Collaborative Learning: The lessons in this curriculum have been developed to include some collaborative learning opportunities. Rather than presenting all information in lecture format and teacher driven, the activities involve the students in a more engaged manner.

Groups: Some of the lessons are carried out in groups. While it isn't necessary for students to remain in the same groups the entire unit, if they work well together, it may foster students to think deeper as they are comfortable with their teammates and willing to ask questions of each other.

Inquiry-based: The lessons in the curriculum invite students to be engaged and ask questions. They work through background information in a guided fashion, but are challenged to think beyond what they have read or done. The teacher serves as the facilitator in these activities, not the deliverer of information.

Technology: Lessons have been written to be mindful of varying availability of technology in schools and homes. Some of the lessons would be very well suited to online environments and if your students are able, you might wish to engage in some of the technology modifications.

Content: Often we teach in a manner that is very content heavy. With high-stakes testing the norm, students are pushed to memorize and regurgitate numerous isolated facts. There is so much content that must be covered in a biology class, for example, that often it is difficult to synthesize those discrete facts into a compelling context or a story. This unit provides that opportunity: to take concepts learned such as the central dogma of molecular biology and transcription in particular, and put them in the context of a familiar example – monozygotic twins. The lessons are designed to teach students *why* these concepts are important and *how* they can be used by researchers.

Implementation notes: This curriculum should be modified and adapted to suit the needs of the teacher and students. To help make implementation easier in this first draft, notes have been included in lessons as needed.

Extensions: For those teaching the AP Biology curriculum, restriction enzyme digest and gel electrophoresis is a necessary laboratory activity. The Arabidopsis DNA Methylation laboratory activity suggested with this lesson includes DNA analysis using PCR, restriction enzyme digest and gel electrophoresis meeting instructional content needs. Additional activities including BLAST and 3D protein modeling can be developed and included with the Epigenetics theme.

Science Subject: Biology

Grade and ability level: 9-12 students in advanced biology

Science concepts: enzymes, DNA, mutations, replication, transcription, transcription factors, translation, protein structure, protein function, genetics, epigenetics, gene switches, methylation, phenotypic expression, cell structure

LESSON SUMMARIES

Lesson One:

Same But Different – How epigenetics can blur the line between nature and nurture

The author's mother and her twin are a study in difference and identity. Monozygotic (MZ) twins born with identical genomes but apparent personality differences and eventual epigenetic divergence provide a starting point for teaching students background knowledge on epigenetics. The history of epigenetics and the basic biochemistry behind the concept are encompassed in the article. After reading the article, students will collaborate in groups to develop a series of interview questions for a pair of monozygotic twins. The questions should probe for the presence of phenotypic ally expressed, observable traits linked to behavior, diet or physical appearance. The questions will be compiled into a master list to be used to electronically interview a pair of MZ twin children and a pair of MZ twin adults. The electronic interview will be sent to the parent of the MZ twin children and each MZ twin adult. Responses will be compared to see if there is a difference in the number of convergent answers between the two MZ twin age groups. MZ twins to be interviewed will be identified by the teacher before the assignment.

Lesson Two:

A Tale of Two Mice

Students will view an online video about a pair of MZ twin mice called the Agouti Sisters. The video content explores a pair of twin mice with obvious epigenetic divergence. Their phenotypic expression has been impacted by environmental exposures in a controlled, laboratory setting. The science behind the epigenome is explained and relevance to the nature vs. nurture controversy is addressed. After watching the video, students complete an assessment based on questions that probe their understanding of the concepts presented.

Lesson Three:

Gene Switches

Gene activity influences phenotypic expression. In this collaborative investigation, students will explore how bacteria may turn genes off or on. Students will model a gene switch in bacteria and the action of an operon that regulates gene expression. This two-part modeling exercise uses a variety of hands-on manipulatives to assist students in visualizing the gene switch concept. A teacher-led discussion will explain how gene switches may occur due to transcription factors or epigenetic influence.

Lesson Four:

Detecting Epigenetic DNA Methylation in Arabidopsis

Students will begin this activity preparation weeks in advance due to the need for flowering Arabidopsis thaliana plants. Phenotypic variance will be observed in the plants. Further investigation will include DNA extraction, restriction enzyme digest, PCR, gel electrophoresis, and bioinformatics to investigate the role of DNA methylation in gene regulation. Students will work in collaborative groups to follow protocol and complete the laboratory assessment.

LESSON SEQUENCING GUIDE

Since the classroom teacher knows his or her students best, the teacher should decide the sequencing of lessons. Below is a suggested pacing guide that can be used when planning to use this curriculum.

50 minute periods

	Day 1	Day 2	Day 3	Day 4	Day 5
Week 1	Lesson 1 **Same But Different** Students will read article. (20 minutes) Students will organize into collaborative groups to discuss the article and write interview questions. (30 minutes)	Lesson 1 **Same But Different** **(Continued)** Teacher will provide each group with MZ twin responses from yesterday's interview questions. Students will discuss the results. (15 minutes) Students will complete collaborative analysis of interview responses in order to determine difference in convergent answers between MZ twin pairs (child/adult). (35 minutes)	Lesson 2 **A Tale of Two Mice and Epigenetics** Students will watch audio slide show followed by Epigenetics video. (20 minutes) Content assessment of video and slide show. (30 minutes)	Lesson 3 **Gene Switches** Teacher-led discussion about genetic and epigenetic gene switches (10 minutes) Student activity using hands-on manipulatives to model gene switches in bacteria and an operon model with written assessment. (40 minutes)	Lesson 4 **Detecting Epigenetic DNA Methylation in Arabidopsis*** Students work in collaborative laboratory groups to investigate phenotypic expression and DNA methylation in plants. Activity requires prior class time to plant and care for Arabidopsis plants and extended lab time for investigation. *extended lab time beyond 50 minutes required.

VOCABULARY

Deletion: removal of one or more nucleotides from a DNA sequence, which may alter the reading frame

DNA: Deoxyribonucleic acid is a nucleic acid containing the genetic instructions used in the development and functioning of all known living organisms.

Enzyme: Enzymes are proteins that catalyze (i.e., increase the rates of) chemical reactions. Almost all chemical reactions in a biological cell need enzymes in order to occur at rates sufficient for life.

Enzyme replacement therapy (ERT): a medical treatment replacing an enzyme in patients in whom that particular enzyme is deficient or absent. Usually this is done by giving the patient an intravenous (IV) infusion containing the enzyme. Enzyme replacement therapy does not "treat" the underlying disease, only the symptoms.

Genotype: The genotype is the genetic makeup of a cell, an organism, or an individual (i.e. the specific allele makeup of the individual). The genotype of an organism is the inherited instructions it carries within its genetic code.

Grand rounds are an important teaching tool and ritual of medical education and inpatient care, consisting of presenting the medical problems and treatment of a particular patient to an audience consisting of doctors, residents and medical students. The patient was traditionally present for the round and would answer questions; grand rounds have evolved with most sessions now rarely having a patient present and being more like lectures.

Insertion: addition of one or more nucleotides in a DNA sequence, which may alter the reading frame

Lysosome: Lysosomes are cellular organelles that contain acidic digestive enzymes to break down waste materials and cellular debris.

Missense: generally a single nucleotide change in the protein coding region that results in a stop codon, causing the protein to be truncated

Nonsense: generally a single nucleotide change in the protein coding region that results in a different amino acid

Peer-review is the act of having another writer read what you have written and respond in terms of its effectiveness. This reader attempts to identify the writing's strengths and weaknesses, particularly reading how sound the science is, and then suggests strategies for revising it. The hope is that not only will the specific piece of writing be improved, but that future writing attempts will also be more successful. Peer-review happens with all types of writing, at any stage of the process, and with all levels of writers.

Pharmacological chaperone: Small molecules that selectively bind to and stabilize proteins in cells, leading to improved protein folding and trafficking, and increased activity.

Phenotype: An organism's observable characteristics or traits. Phenotypes result from the expression of an organism's genes as well as the influence of environmental factors and the interactions between the two.

Pompe disease: Pompe disease is an inherited disorder caused by the buildup of a complex sugar called glycogen in the body's cells. The accumulation of glycogen in certain organs and tissues, especially muscles, impairs their ability to function normally. There are three types of Pompe disease, which differ in severity and the age at which they appear. These types are known as classic infantile-onset, non-classic infantile-onset, and late-onset.

Reading frame: a way of breaking a sequence of nucleotides in DNA or RNA into three letter codons, resulting in a possibility of three reading frames in mRNA and six in double-stranded DNA (since have forward and reverse).

RNA: Ribonucleic acid is one of the three major macromolecules (along with DNA and proteins) that are essential for all known forms of life. Like DNA, RNA is made up of a long chain of components called nucleotides. Each nucleotide consists of a nucleobase, a ribose sugar, and a phosphate group. RNA directs the synthesis of proteins.

Transcription: DNA → RNA; During transcription, a DNA sequence is read by an RNA polymerase, which produces a complementary, antiparallel RNA strand. The RNA complement includes uracil (U) in all instances where thymine (T) would have occurred in a DNA complement.

Translation: RNA → Protein; In translation, messenger RNA (mRNA) produced by transcription is decoded by the ribosome to produce a specific amino acid chain, or polypeptide, that will later fold into an active protein.

CURRICULUM SUMMARY

The course unit of focus will be AP Biology – ***Unit 6: Biotechnology and Gene Activity***. When I initially wrote the curriculum used for this unit, the background content was viewed as general support for the study of biotechnology. I always felt that the background content was weak and lacked sufficient detail for students to truly grasp DNA replication, transcription, translation, protein synthesis and gene expression. The unit encompasses three chapters of content: Molecular Biology of the Gene, Regulation of Gene Expression, and Biotechnology and Genomics. The background content and supporting activities associated with the unit will be completely changed in terms of depth of content for student understanding and more student activities that assess their knowledge of the content. My students have typically studied the background content with disdain and complained that it was "so boring". The concept of epigenetic inheritance has the potential to help students have an increased desire to understand molecular biology of the gene and gene expression with "hooks" based on articles of interest. The part of this unit students seemed to grasp best was the information associated with mutations. Therefore, I will rewrite the unit with *Epigenetic Inheritance* as a major theme (a topic discussed by definition only in the past). DNA replication, transcription, translation and protein synthesis will be incorporated as the "tool" to understand how epigenetic inheritance works and much greater detail will be given to the instruction of mutations, types of mutations, how they work, and diseases and disorders that can result. Since the majority of my AP Biology students took my AP Environmental Science class the previous year, they have background knowledge regarding chemicals in the environment. I will use environmental chemical exposure to substances such as BPA to illustrate how epigenetic inheritance can result from chemical exposure. The entire unit normally lasts a little over three weeks. For the purpose of this assignment, I will focus on the following concepts: epigenetic inheritance, mutations, and exposure to environmental substances that impact genetic code.

Learning outcomes linked to standards:

Essential questions – What is epigenetic inheritance? How do mutations occur and how do they change genetic instructions? How can exposure to environmental substances impact genetic code?

Learning Goals –

*Students will review and understand the process of DNA replication, transcription, and translation.

*Students will learn the meaning of epigenetic inheritance and how it is possible for genes to turn off and on.

*Students will learn how mutations occur to change the genetic code of a cell and what the outcome of those changes mean to an organism as it can translate to disease and disorder.

*Students will learn examples of chemical substances that may have epigenetic impact on an organism.

Florida Standards –

SC.912.L.16.3 – ***Describe the basic process of DNA replication and how it relates to the transmission and conservation of the genetic information.***

Standard: Heredity and Reproduction

SC.912.L.15.15 – ***Describe how mutations and genetic recombination increase genetic variation***.

Standard: Heredity and Reproduction

SC.912.L.16.4 – ***Explain how mutations in the DNA sequence may or may not result in phenotypic change in offspring.***

Standard: Diversity and Evolution of Living Organisms

AP Biology Big Ideas and Learning Objectives –

Big Idea 3: Living systems store, retrieve, transmit and respond to information essential to life processes.

Enduring Understanding A: Heritable information provides for continuity of life.

Essential Knowledge 1: DNA and in some cases RNA, is the primary source of heritable information.

Enduring Understanding B: Expression of genetic information involves cellular and molecular mechanisms.

Essential Knowledge 1: Gene regulation results in differential gene expression, leading to cell specialization.

Big Idea 4: Biological systems interact, and these systems and their interactions possess complex properties.

Enduring Understanding C: Naturally occurring diversity among and between components within biological systems affects interactions with the environment.

Essential Knowledge 2: Environmental factors influence the expression of the genotype in an organism.

LO 4.24 The student is able to predict the effects of a change in an environmental factor on genotypic expression.

Learning Performance Ideas :

*Students will identify steps in process of DNA replication, transcription and translation as well as complete a reinforcement activity.

*Students will read article on twin studies and epigenetic inheritance. Assessment with article.

*Students will learn the role of methylation in epigenetics and its impact on organisms. Lab – Detecting Epigenetic DNA Methylation in Arabidopsis Amplification and Electrophoresis Kit #211404P?

*Students will learn that genes can switch “off” and “on” and mechanisms that cause gene switching; Science Take-Out?

*Students will use a DNA sequence, convert to mRNA sequence and amino acid sequence for normal and mutated examples. Sickle Cell Anemia will be used as an example mutation as well as an environmental chemical example (to be determined, prefer BPA).

BACKGROUND INFORMATION

In the 1940's, Conrad H. Waddington, an English embryologist, suggested that cells acquired their identities by *nurture* modifying *nature*. He said *nurture* originated from environmental signals. Waddington concluded that a mysterious, ghostlike layer of "memory" hovered in cells to record the past and establish the cell's future while permitting that future to be changed. He coined the term *epigenetics*, meaning "above genetics". The definition of epigenetics in the words of Waddington (1942) was, "the branch of biology which studies the causal interactions between genes and their products, which bring the phenotype into being".

For many years, the term was somewhat forgotten. However, today, *epigenetics* is witnessing a revival. Molecular biologists, biochemists and geneticists around the globe are working on epigenetic research converging on the study of modifications of DNA and histone proteins and the mechanisms by which such modifications influence overall chromatin structure. Genes may turn "on" or "off", evidence that the genetic blueprint of a cell is not passive. Genes may be activated or repressed as a result of signals that impact their expression.

An interesting way to research epigenetic characteristics is through the study of monozygotic twins. Monozygotic twins are nature's clones which result from a single fertilized egg that has divided into two identical embryos. Both embryos are of the same sex and possess identical genetic codes or genomes. Approximately one-third of all twins born are monozygotic. Over time, characteristics or phenotypic expressions of these twins may diverge. Due to environmental signals, different genes may turn "off" or "on" leading to pronounced differences in behavior or health. For example, just because one twin develops diabetes or cancer, does not mean the other twin will develop the same disease. Over the course of a life time, the twins may live or work in different locations creating a difference in exposure to environmental signals. Diets, behavioral habits, and stress-levels may vary between the twins leading to different genes being activated or repressed.

DNA methylation is an example of an epigenetic mechanism that may cause genes to switch "off" or "on". The DNA molecule contains four nitrogen bases; adenine, guanine, cytosine and thymine. In the case of eukaryotic cells, cytosine may become "methylated". Adenine may become methylated in prokaryotes. A methyl group (CH_3), when attached to a cytosine base, becomes 5-methylcytosine (5-mC) and thus modifies gene function. These methyl groups project into the DNA and inhibit transcription. The addition of methyl groups is controlled by a group of enzymes called DNA methyltransferases (DNMTs). Epigenetic reprogramming of genes is controlled by the demethylation process (removal of a methyl group). Demethylation has been associated with various diseases because it is linked to tumor progression. A second DNA base modifier has been found, 5-hydroxymethylcytosine (5-hmC), but is in the early stages of research.

LESSON ONE: SAME BUT DIFFERENT

KEY QUESTION(S): What is epigenetic inheritance? How can environmental factors influence gene expression? How can monozygotic (MZ) twins be used in epigenetic studies?

OVERALL TIME ESTIMATE:

- Advance Preparation: 70 minutes (15 minutes to assemble reading packets; 20 minutes background reading, 15 minutes preparing consolidated interview questions and submitting them to MZ twin volunteers, 20 minutes contact and discussion time with monozygotic twins to be used in interviews)
- Student Procedure: two 50 minute class periods

LEARNING STYLES: Visual and auditory

VOCABULARY:

Epigenetic Inheritance: an inheritance pattern in which a nuclear gene has been modified but the changed expression of the gene may not be permanent over many generations; the transmission of genetic information by means that are not based on the coding sequences of a gene.

Monozygotic Twins: also known as identical twins; form from a single fertilized egg and possess the same genome.

Histones: group of proteins involved in forming the nucleosome structure of eukaryotic chromatin.

Enzyme: Enzymes are proteins that catalyze (i.e., increase the rates of) chemical reactions. Almost all chemical reactions including biochemical pathways in a biological cell need enzymes in order to occur at rates sufficient for life.

DNA Methyltransferase: family of enzymes that catalyze the transfer of a methyl group to DNA.

DNA: Deoxyribonucleic acid is a nucleic acid containing the genetic instructions used in the development and functioning of all known living organisms. DNA molecules contain four nitrogenous bases; adenine, guanine, cytosine and thymine.

DNA Methylation: process by which methyl groups ($-CH_3$) are added to nuclear DNA; attach to cytosine.

LESSON SUMMARY:

In the article selected for the lesson, the author's mother and her twin are a study in difference and identity. Monozygotic (MZ) twins born with identical genomes but apparent personality differences and eventual epigenetic divergence provide a starting point for teaching students background knowledge on epigenetics. The history of epigenetics and the basic biochemistry behind the concept are encompassed in the article. After reading the article, students will collaborate in groups to develop a series of interview questions for monozygotic twins. The questions should probe for the presence of phenotypically expressed, observable traits linked to behavior, diet or physical appearance. The questions will be compiled into a master list to be used to electronically interview a pair of MZ twin children and a pair of MZ twin adults. The electronic interview will be sent to the parent of the MZ twin children (in duplicate) and each MZ twin adult. Responses will be compared to see if there is a difference in the number of convergent answers between the two MZ twin age groups. MZ twins to be interviewed will be identified by the teacher before the assignment.

STUDENT LEARNING OBJECTIVES: The student will be able to……

1. Explain epigenetic inheritance.
2. Explain the role of histone modification and DNA methylation in the epigenome.
3. Describe why monozygotic twins can be valuable to epigenetic research.
4. Explain how genes may switch off and on.
5. Describe how gene regulation impacts phenotypic expression.
6. Explain why understanding how the epigenome works could impact disease and drug research.

STANDARDS:

SC.912.L.14.6
SC.912.L.15.15
SC.912.L.16.3
SC.912.L.16.4
SC.912.L.16.5
SC.912.L.18.4
SC.912.L.18.11
SC.912.N.1.1
SC.912.N.1.6
SC.912.N.1.7
HS-LS3-1
AP Biology 3.A.1, 3.B.1, 4.C.2

MATERIALS:

- 1 copy of *Teacher Pages: Article, Same But Different, (Mukherjee), http://www.newyorker.com/magazine/2016/05/02/breakthroughs-in-epigenetics*
- 1 copy of *Teacher Pages: Collaborative Group Questions for Interview of Monozygotic Twins*
- 1 copy of *Teacher Pages: Analysis of Responses to Interview Questions*

- 1 copy of *Student Homework Questions: to be used after reading article, Same But Different, (Mukherjee)*

BACKGROUND INFORMATION: Teachers are encouraged to read the student information (Article: Same But Different - Mukherjee) prior to the activity. This activity specifically focuses on the fundamentals of epigenetic inheritance to help students comprehend what it is so they can better understand how it might impact our future research and treatment of disease, disorder and pharmacology.

ADVANCE PREPARATION:

1. Make copies of article or provide link to online resource. *http://www.newyorker.com/magazine/2016/05/02/breakthroughs-in-epigenetics*

2. Make copies of homework questions reviewing content of the article*: Same But Different Review Guide*
3. Make copies of *Student Worksheet: Collaborative Group Questions for Interview of Monozygotic Twins*
4. Make copies of *Student Worksheet: Analysis of Responses to Interview Questions*
5. Contact parent of pair of monozygotic twin children willing to complete online interview with the children to resubmit responses on specified date, contact pair of monozygotic twin adults willing to complete online interview questions and resubmit responses on specified date.
6. After class turns in student worksheet, *Collaborative Group Questions for Interview of Monozygotic Twin*s, one worksheet per group, consolidate questions and send to participating twins electronically.
7. Make copies of electronic interview responses or provide them to students on day two of lesson in some form. They will need the responses to complete their analysis of responses.

PROCEDURE AND DISCUSSION QUESTIONS WITH TIME ESTIMATES:

1. (20 minutes) Ask students to read ***Same But Different – How epigenetics can blur the line between nature and nurture***, by Siddhartha Mukherjee.
2. (30 minutes) Ask the class to assemble into groups of 3-4 students - teacher may wish to select groups – in order to collaborate in producing 15 questions about phenotypic expression related to human behavior, diet and physical appearance. Provide students with handout: *Collaborative Group Questions for Interview of Monozygotic Twins.*
3. (0 minutes) Provide students with homework questions to review content of article: *Same But Different Review Guide.* Answers to questions should be submitted to teacher the following day (due date may vary with teacher discretion).
4. (15 minutes) Teacher will provide each group of students with a copy of the online interview responses from the two sets of MZ twins. Group will review and discuss the responses.
5. (35 minutes) Student groups will work to analyze the responses to interview questions, complete student worksheet, one per group.

ASSESSMENT SUGGESTIONS:

- *Collaborative Group Questions for Interview of Monozygotic Twins* can be graded for completion. When consolidating questions for the online interview, you may use five questions from each of the three question categories (behavior, diet, and physical appearance). Therefore, some of the questions written by the students will not be used.
- *Same But Different Review Guide* should be graded for accuracy.
- If class time remains when *Analysis of Responses to Interview Questions* is completed by each group, discuss the results.

EXTENSIONS:

Additional articles can be read for greater depth of understanding:

1. http://discovermagazine.com/2013/may/13-grandmas-experiences-leave-epigenetic-mark-on-your-genes
2. http://blogs.discovermagazine.com/d-brief/2013/05/09/how-twin-mice-develop-different-personalities/#.V4RYs_krLIU
3. http://jeb.biologists.org/content/218/1/134
4. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3063335/

RESOURCES/REFERENCES:

1. Article of focus: ***Same But Different – How epigenetics can blur the line between nature and nurture***, Siddartha Mukherjee, *http://www.newyorker.com/magazine/2016/05/02/breakthroughs-in-epigenetics*.
2. Website of epigenetic videos and resources: http://learn.genetics.utah.edu/content/epigenetics/

TEACHER PAGES: *COLLABORATIVE GROUP QUESTIONS FOR INTERVIEW OF MONOZYGOTIC TWINS.*

Questions for Interview of Monozygotic Twins

Group Members: _____

_____

A. Write 5 questions regarding a phenotypic behavior (for example: Do you play with your hair when you get nervous?)

1. _____

   _____
2. _____

   _____
3. _____

   _____
4. _____

_____

5. _____

_____

B. Write 5 questions regarding dietary habits or preferences (for example: Would he prefer to eat a chocolate snack or chips?)

1. _____

_____

2. _____

_____

3. _____

_____

4. _____

_____

5. _____

C. Write 5 questions regarding physical appearance (for example: Do you have attached or free ear lobes?)

1. _____

_____

2. _____

_____

3. _____

_____

4. _____

_____

_____

_____

Same But Different – How epigenetics can blur the line between nature and nurture:

Review Guide

Name _____ Date _____

1. Twins Bulu and Tulu were born in Delhi in 1942. Bulu was beautiful, placid and _____, while Tulu came squirming and squalling.

   a. lactose intolerant b. undernourished c. hot-tempered d. healthy

2. Tulu enjoyed theater and _____ but Bulu was a writer and dreamer.

   a. poetry b. music c. dancing d. reading

3. Tulu and Bulu both entered into arranged marriages. How were their husbands different?

   _____

   _____

   _____

   _____

4. Identical twins separated at birth rarely have converged characteristics?

   a. True b. False

5. David Allis has an identical twin sister.

   a. True b. False

6. In the 1940's, _____ proposed that cells acquired their identities just as humans do by letting nurture modify nature.

   a. Conrad Waddington b. Karl Marx c. David Allis d. Danny Reinberg

7. The selective activation or _____ of genes allows an individual cell to acquire its identity.

a. passivity b. memory c. identity d. repression

8. What was special about the microbe *Tetrahymena*? _____

_____

_____

9. DNA wraps around a core of proteins called _____.

10. What insect was used to study chemical effects on the brain?

_____

11. Malignant cells have aberrant patterns of DNA methylation or histone modification. Therefore, epigenetic information must play a role in _____.

12. Epigenetic _____ target methylation and histone modification.

a. drugs b. memories c. identities d. imprinting

13. Transgenerational epigenetic transmission is not possible.

a. True b. False

14. Darwin discredited the work of _____ but epigenetic research is reviving some of his theories.

a. Allis b. Yamanaka c. Lamarck d. Reinberg

15. The individuality of an organism is suspended somewhere between genome and _____.

Analysis of Responses to Interview Questions

Name _____ Date _____

A. Number of convergent responses to behavioral phenotypes.

1. MZ twins – children _____
2. MZ twins – adults _____

B. Number of convergent responses to diet phenotypes.

1. MZ twins – children _____
2. MZ twins – adults _____

C. Number of convergent responses to physical appearance.

1. MZ twins – children _____
2. MZ twins – adults _____

D. On a separate sheet of paper, graph your results.

E. On a separate sheet of paper, explain your findings.

TEACHER PAGES: ANSWER KEY- SAME BUT DIFFERENT REVIEW GUIDE

Same But Different – How epigenetics can blur the line between nature and nurture:

Review Guide

Name _____ Date _____

1. Twins Bulu and Tulu were born in Delhi in 1942. Bulu was beautiful, placid and _____, while Tulu came squirming and squalling.

   a. lactose intolerant b. undernourished c. hot-tempered d. healthy

2. Tulu enjoyed theater and _____ but Bulu was a writer and dreamer.

   a. poetry b. music c. dancing d. reading

3. Tulu and Bulu both entered into arranged marriages. How were their husbands different?

   Tulu married a penniless immigrant, but became very prosperous allowing the family to take expensive vacations and providiing her children with positive cultural experiences. Bulu married a lawyer who kept up the appearances of working but did not prosper requiring the family to move to a 3-room flat.

4. Identical twins separated at birth rarely have converged characteristics?

   a. True b. False

5. David Allis has an identical twin sister.

   a. True b. False

6. In the 1940's, _____ proposed that cells acquired their identities just as humans do by letting nurture modify nature.

   a. Conrad Waddington b. Karl Marx c. David Allis d. Danny Reinberg

7. The selective activation or _____ of genes allows an individual cell to acquire its identity.

a. passivity b. memory c. identity d. repression

8. What was special about the microbe *Tetrahymena*?

Tetrahymena is a single-celled, ciliated microbe. It carries two distinct collections of genes. One shut off and the other turned on. The mechanism for this was found to be histone modification.

9. DNA wraps around a core of proteins called histones.

10. What insect was used to study chemical effects on the brain? ant

11. Malignant cells have aberrant patterns of DNA methylation or histone modification. Therefore, epigenetic information must play a role in cancer .

12. Epigenetic _____ target methylation and histone modification.

a. drugs b. memories c. identities d. imprinting

13. Transgenerational epigenetic transmission is not possible.

a. True b. False

14. Darwin discredited the work of _____ but epigenetic research is reviving some of his theories.

a. Allis b. Yamanaka c. Lamarck d. Reinberg

15. The individuality of an organism is suspended somewhere between genome and epigenome.

LESSON TWO: EPIGENETICS AND A TALE OF TWO MICE

KEY QUESTION(S): What is epigenetic inheritance? How can environmental factors influence gene expression? How can monozygotic (MZ) twins be used in epigenetic studies? What is the impact of methylation on the Agouti gene?

OVERALL TIME ESTIMATE:

- Advance Preparation: 20 minutes (10 minutes to set up technology for audio/video; 10 minutes to make copies of Student Worksheet)
- Student Procedure: one 40- 50 minute class period

LEARNING STYLES: Visual and auditory

VOCABULARY:

Epigenetic Inheritance: an inheritance pattern in which a nuclear gene has been modified but the changed expression of the gene may not be permanent over many generations; the transmission of genetic information by means that are not based on the coding sequences of a gene.

Monozygotic Twins: also known as identical twins; form from a single fertilized egg and possess the same genome.

Gene Expression: appearance in a phenotype of a characteristic or effect attributed to a particular gene.

Differentiation: specialization in the structure or function of a cell typically caused by the activation of specific genes.

Epigenome: consists of a record of the chemical changes to the DNA and histone proteins of an organism; involved in regulating gene expression, development, tissue differentiation, and currently an active topic in cancer research.

Agouti gene: responsible for determining whether a mammal's coat is banded (*agouti*) or of a solid color (*non-agouti*).

LESSON SUMMARY:

Students will view an online audio slide show about a pair of MZ twin mice called the Agouti Sisters. The slide show explores a pair of twin mice with obvious epigenetic divergence. Their phenotypic expression has been impacted by environmental exposures in a controlled, laboratory setting. The science behind the epigenome is explained and relevance to the nature vs. nurture controversy is addressed. The slide show is followed by a video on Epigenetics (same website). After watching the video, students complete an assessment based on questions that probe their understanding of the concepts presented.

STUDENT LEARNING OBJECTIVES: The student will be able to……

7. Explain epigenetic inheritance.
8. Explain the role of histone modification and DNA methylation in the epigenome.
9. Describe why monozygotic twins can be valuable to epigenetic research.
10. Explain how genes may switch off and on.
11. Describe how gene regulation impacts phenotypic expression.
12. Explain that exposure to chemicals in the environment may trigger gene switches.
13. Explain why understanding how the epigenome works could impact disease research, particularly cancer.

STANDARDS:

Florida Standards: SC.912.L.14.6

SC.912.L.15.15

SC.912.L.16.3

SC.912.L.16.4

SC.912.L.16.5

SC.912.L.18.4

SC.912.L.18.11

SC.912.N.1.1

SC.912.N.1.6

SC.912.N.1.7

AP Biology 3.A.1, 3.B.1, 4.C.2

National Standards - Benchmarks for Science Literacy

6B/H4 (Grades: 9-12): The development and use of technologies to sustain, prolong, or terminate life raise social, moral, ethical, and legal issues.

8F/H7 (Grades: 9-12): Biotechnology has contributed to health improvement in many ways, but its cost and application have led to a variety of controversial social and ethical issues.

NSTA National Science Education Standards

C.2.1 (Grades: 9-12): In all organisms, the instructions for specifying the characteristics of the organism are carried in DNA, a large polymer formed from subunits of four kinds (A, G, C, and T). The chemical and structural properties of DNA explain how the genetic information that underlies heredity is both encoded in genes (as a string of molecular "letters") and replicated (by a templating mechanism). Each DNA molecule in a cell forms a single chromosome.

C.2.2 (Grades: 9-12): Most of the cells in a human contain two copies of each of 22 different chromosomes. In addition, there is a pair of chromosomes that determines sex: a female contains two X chromosomes and a male contains one X and one Y chromosome. Transmission of genetic information to offspring occurs through egg and sperm cells that contain only one representative from each chromosome pair. An egg and a sperm unite to form a new individual. The fact that the human body is formed from cells that contain two copies of each chromosome--and therefore two copies of each gene--explains many features of human heredity, such as how variations that are hidden in one generation can be expressed in the next.

MATERIALS:

- Technological access to a website to obtain an audio slide show and video. Students must be able to view by electronic device or classroom projection.
- 1 copy of *Teacher Pages: Transcript of Audio Slide Show – A Tale of Two Mice*
- 1 copy of *Teacher Pages: Transcript of Video - Epigenetics*

- 1 copy of *Teacher Pages: Student Worksheet to be filled in as student interactively views slide show, "A Tale of Two Mice", and video on "Epigenetics".*
- 1 copy of *Teacher Pages: Answer Key for Student Worksheet*

BACKGROUND INFORMATION: In the audio slide show (A Tale of Two Mice), Dr. Dana Dolinoy of Duke University explains the role that the epigenome, a sort of second genome, plays in regulating the expression of our genes. As Dolinoy notes, we can no longer say with certainty whether genetics or the environment have a greater impact on our health, because the two are inextricably linked through the epigenome. In the (Epigenetics) video, it points out that once nurture seemed clearly distinct from nature. Now it appears that our diets and lifestyles can change the expression of our genes by influencing a network of chemical switches within our cells collectively known as the epigenome. This new understanding may lead us to potent new medical therapies. Epigenetic cancer therapy, for one, already seems to be yielding promising results.

ADVANCE PREPARATION:

8. Prepare technology for classroom viewing or provide link to online resource to students for the auditory slide show "A Tale of Two Mice": http://www.pbs.org/wgbh/nova/body/epigenetic-mice.html

9. Prepare technology for classroom viewing or provide link to online resource to students for a brief video, "Epigenetics", http://www.pbs.org/wgbh/nova/body/epigenetics.html

10. Make copies of *Student Worksheet: to be filled in as student interactively views slide show, "A Tale of Two Mice", and video on"Epigenetics".*

PROCEDURE AND DISCUSSION QUESTIONS WITH TIME ESTIMATES:

6. (15-20 minutes) – The interactive audio slide show, "A Tale of Two Mice", takes about 5 minutes to view. Following the slide show, provide the students with time to think about the information they viewed and answer the extended response question about methylated vs. non-methylated DNA.

7. (15-20 minutes) - The "Epigenetics" video, takes about 15 minutes to view. Students will need to fill in the blanks as they watch the video.

8. (10 minutes) – After students submit their worksheet over the slide show/video, take time to allow for a "whole class discussion" to express views on what they have just seen. For teachers preferring a more structured use of possible remaining time, view the tutorial on the same website called "Gene Switches". This will be a good introduction for tomorrow's activity.

ASSESSMENT SUGGESTIONS:

- Student worksheet may be graded for accuracy or completion as a class work grade.

EXTENSIONS:

A. Additional video –" The Ghost in Your Genes", NOVA, 2008
Identical twins share the same genes and are often startlingly alike. Why, then, should they often meet such different fates one twin developing a serious disease like cancer while the other remains unscathed? In a compelling scientific detective story, The Ghost in Your Genes explores the provocative idea that there may be more to inheritance than genes alone. New clues reveal that a second epigenetic chemical code sits on top of our regular DNA and controls how our genes are expressed, turning them on or off with dramatic consequences for our health.

This revolutionary finding has vital implications not only for treating disease but for how we take care of

ourselves. While we inherit the epigenome much as we do DNA, it appears to respond far more to our environment and lifestyles. So our stress levels and what we eat, drink, and breathe may leave an enduring imprint, not just on our own bodies but on the generations to come. In a tour-de-force of scientific sleuthing, NOVA reveals the discoveries that have overturned the old story of inheritance and have profound relevance for how we choose to lead our lives.

Additional articles can be read for greater depth of understanding:

5. http://discovermagazine.com/2013/may/13-grandmas-experiences-leave-epigenetic-mark-on-your-genes
6. http://blogs.discovermagazine.com/d-brief/2013/05/09/how-twin-mice-develop-different-personalities/#.V4RYs_krLIU
7. http://jeb.biologists.org/content/218/1/134
8. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3063335/

RESOURCES/REFERENCES:

3. *PBS/NOVA Website of Epigenetic Resources: http://www.pbs.org/wgbh/nova/genes/*

4. Website of epigenetic videos and resources: http://learn.genetics.utah.edu/content/epigenetics/

TEACHER PAGES: TRANSCRIPT “A TALE OF TWO MICE”

CHAPTER 1: THE AGOUTI SISTERS

DANA DOLINOY: Hi, I'm Dr. Dana Dolinoy, a post-doctoral research fellow in the laboratory of Randy Jirtle at Duke University. In our laboratory we study epigenetic gene regulation, or how environmental exposures interact with the epigenome to affect long-term health and disease.

So today I'd like to introduce you to two Agouti mice. And as you can see, the yellow mouse is quite obese, and she is also prone to diabetes and cancer. But on the other hand, the brown mouse remains slender and lean and also has a lower risk of developing disease. But what's really amazing about these two mice are that they are genetically identical — they are two identical twin sisters from the same mother. So what makes them look so different?

CHAPTER 2: THE EPIGENOME

DANA DOLINOY: Well, it turns out that there's a second genome called the epigenome. Epigenome literally means, in addition to, or above, the genome, and while the recently completed human genome project identified approximately 25,000 genes, these genes still need instructions for what to do and when to do it and where to do it, and that's where the epigenome comes into play.

A useful analogy is to think of the epigenome as the software that directs the genomic hardware of a computer. All of our cells contain the same DNA and genes, but it is the epigenome that decides how these genes are expressed and determines how a cell becomes a heart cell, a liver cell or even a hair cell.

Epigenetics consists of molecular switches and markers, such as DNA methylation, that help control gene regulation in which a quartet of atoms called a methyl group attaches to DNA and shuts down genes. And as you can see the red balls here are attaching to the DNA and turning off the gene.

CHAPTER 3: THE ELUSIVE AGOUTI

DANA DOLINOY: So back to the Agouti sisters. In the yellow obese mouse, the Agouti gene is unmethylated and turned on all the time, while in the brown mouse, the gene is completely methylated and shut down. There are also other mice that appear mottled in which half of the cells are methylated and shut down, and the other half are unmethylated and turned on, and these mice appear to be yellow and brown. So the coat colors of these Agouti mice acts like a sensor for the amount of DNA methylation present.

We used the Agouti mice to study how maternal nutrients and environmental factors affect the epigenome. Specifically, we wanted to know whether a mom's exposure to a contaminant found everywhere in the environment can alter the fetal epigenome, and eventually the long-term fate of her offspring.

In the study, pregnant mothers were exposed to a common chemical found in certain plastics. This chemical is called bisphenol-A, or BPA for short, and it's present in many commonly used products, including food and beverage containers, baby bottles, dental sealants and the lining of food cans.

About four years ago, the CDC studied approximately 400 people, and in 95 percent of these 400 people, they measured detectable levels of bisphenol-A.

And when we fed the pregnant mothers, the mice, BPA, we noticed that the number of offspring with the yellow obese coat color increased dramatically, and we also saw that maternal exposure to this chemical decreased DNA methylation in the offspring and turned this Agouti gene on when it is supposed to be off.

CHAPTER 4: BREEDING HEALTHY PUPS

DANA DOLINOY: So we started a second study in which pregnant mothers were exposed to BPA plus nutritional supplementation such as methyl donors like folic acid or genistein, which is a common ingredient found in soy products. The level of soy that we provided is similar to what a person who eats a high soy diet or an individual living in Asia might eat.

And once we did this, we observed that the offspring were no longer predominantly yellow and more obese, and that there were more offspring with the slender brown coat color phenotype. This indicates that maternal nutrient supplementation can counteract the negative effects of exposure to that chemical.

CHAPTER 5: CONCLUSIONS

DANA DOLINOY: The traditional thinking about human health and disease is that it is affected by genetics and the environment, and whenever identical twins have different disease status, this was often attributed to the environment or different behavioral choices such as smoking status.

But with epigenetic gene regulation, we can see that we can no longer say whether genetics or the environment have a bigger impact, because it may be not only what you were exposed to, but what your mother and potentially grandparents were exposed to as well. And maybe even your father.

These studies with the agouti mice show us that we can no longer say whether genetics or the environment have a greater impact on our health, because the two are inextricably linked through the epigenome. This work suggests in the future that we may be able to protect individuals from negative epigenetic profiles, either by modifying the diet or developing drugs that can affect epigenomic profiles, although we're several years away from doing this.

NEIL DEGRASSE TYSON: Did you ever notice that if you get to know two identical twins, they might look alike, but they're always subtly different?

CANTANKEROUS NEIL DEGRASSE TYSON: Yep, whatever.

CHEERFUL NEIL DEGRASSE TYSON: As they get older, those differences can get more pronounced. Two people start out the same but their appearance and their health can diverge. For instance, you have more gray hair.

CANTANKEROUS NEIL DEGRASSE TYSON: No. No, I don't. Identical twins have the same DNA, exact same genes.

CHEERFUL NEIL DEGRASSE TYSON: Yeah.

CANTANKEROUS NEIL DEGRASSE TYSON: And don't our genes make us who we are?

CHEERFUL NEIL DEGRASSE TYSON: Well they do, yes, but they're not the whole story. Some researchers have discovered a new bit of biology that can work with our genes or against them.

CANTANKEROUS NEIL DEGRASSE TYSON: Yeah, you're heavier, and I'm better looking.

CHEERFUL NEIL DEGRASSE TYSON: Yeah, whatever.

NEIL DEGRASSE TYSON: Imagine coming into the world with a person so like yourself, that for a time you don't understand mirrors.

CONCEPCIÍ“N: As a child, when I looked in the mirror I'd say, "That's my sister." And my mother would say, "No, that's your reflection!"

NEIL DEGRASSE TYSON: And even if you resist this cookie-cutter existence, cultivate individual styles and abilities—like cutting your hair differently, or running faster—uncanny similarities bond you together: facial expressions, body language, the way you laugh—or dress for an interview, perhaps, when you hadn't a clue what your sister was going to wear. The synchrony in your lives constantly confronts you.

CLOTILDE: When I see my sister, I see myself. If she looks good, I think, "I look pretty today." But if she's not wearing makeup, I say, "My god, I look horrible!"

NEIL DEGRASSE TYSON: It's hardly surprising because you both come from the same egg. You have precisely the same genes. And you are literally clones, better known, as identical twins.

But now, imagine this: one day, your twin, your clone, is diagnosed with cancer. If you're the other twin, what can you do except wait for the symptoms?

CLOTILDE: I have been told that I am a high risk for cancer. Damocles' sword hangs over me.

NEIL DEGRASSE TYSON: And yet, it's not uncommon for a twin, like Ana Mari, to get a dread disease, while the other, like Clotilde, doesn't. But how can two people so alike, be so unalike?

Well, these mice may hold a clue. Their DNA is as identical as Ana Mari and Clotilde's despite the differences in their color and size. The human who studies them is Duke University's Randy Jirtle.

So, Randy, I see here you have skinny mice and fat mice. What have you done in this lab?

RANDY JIRTLE: Well, these animals are actually genetically identical.

NEIL DEGRASSE TYSON: The fat ones and the skinny ones?

RANDY JIRTLE: That's correct.

NEIL DEGRASSE TYSON: Because these are huge.

RANDY JIRTLE: They're huge.

NEIL DEGRASSE TYSON: Can we weigh them and find out?

RANDY JIRTLE: Sure. So if you take this...

NEIL DEGRASSE TYSON: It looks like they can barely walk.

RANDY JIRTLE: They can't walk too much. They're not going to be running very far. So that's about 63 grams.

NEIL DEGRASSE TYSON: 63 grams.

RANDY JIRTLE: Let's look at the other one.

NEIL DEGRASSE TYSON: So it's half the weight.

RANDY JIRTLE: Right.

NEIL DEGRASSE TYSON: This gets even more mysterious when you realize that these identical mice both have a particular gene, called agouti, but in the yellow mouse it stays on all the time, causing obesity.

Just look at this.

So what accounts for the thin mouse? Exercise? Atkins? No, a tiny chemical tag of carbon and hydrogen, called a methyl group, has affixed to the agouti gene, shutting it down. Living creatures possess millions of tags like these. Some, like methyl groups, attach to genes directly, inhibiting their function. Other types grab the proteins, called histones, around which genes coil, and tighten or loosen them to control gene expression. Distinct methylation and histone patterns exist in every cell, constituting a sort of second genome, the epigenome.

RANDY JIRTLE: Epigenetics literally translates into just meaning "above the genome." So if you would think, for example, of the genome as being like a computer, the hardware of a computer, the epigenome would be like the software that tells the computer when to work, how to work, and how much***.***

NEIL DEGRASSE TYSON: In fact, it's the epigenome that tells our cells what sort of cells they should be. Skin? Hair? Heart? You see, all these cells have the same genes. But their epigenomes silence the unneeded ones to make cells different from one another. Epigenetic instructions pass on as cells divide, but they're not necessarily permanent. Researchers think they can change, especially during critical periods like puberty or pregnancy.

Jirtle's mice reveal how the epigenome can be altered. To produce thin, brown mice instead of fat, yellow ones, he feeds pregnant mothers a diet rich in methyl groups to form the tags that can turn genes off.

RANDY JIRTLE: And I think you can see that we dramatically shifted the coat color and we get many, many more brown animals.

NEIL DEGRASSE TYSON: And that matters because your coat color is a tracer, is an indicator...

RANDY JIRTLE: That's correct.

NEIL DEGRASSE TYSON: ...of the fact that you have turned off that gene?

RANDY JIRTLE: That's right.

NEIL DEGRASSE TYSON: This epigenetic fix was also inherited by the next generation of mice, regardless of what their mothers ate. And when an environmental toxin was added to the diet instead of nutrients, more yellow babies were born, doomed to grow fat and sick like their mothers.

It seems to me, this has profound implications for our health.

RANDY JIRTLE: It does, for human health. If there are genes like this in humans, basically, what you eat can affect your future generations. So you're not only what you eat, but potentially what your mother ate, and possibly even what your grandparents ate.

NEIL DEGRASSE TYSON: So how do you go to humans to do this experiment, when you have these mice, and they're genetically identical on purpose?

RANDY JIRTLE: That's right.

NEIL DEGRASSE TYSON: So, who is your perfect lab human?

RANDY JIRTLE: Well, then we look for identical humans, which are identical twins.

NEIL DEGRASSE TYSON: Twins, twins.

And that brings us to the reason why we're showing you Spanish twins. In 2005, they participated in a groundbreaking study in Madrid. Its aim? To show just how identical, epigenetically, they are or aren't.

MANEL ESTELLER (Spanish National Cancer Center): One of the questions of twins is, "If my twin has this disease, I will have the same disease?" And genetics tell us that there is a high risk of developing the same disease. But it's not really sure they are going to have it, because our genes are just part of the story. Something has to regulate these genes, and part of the explanation is epigenetics.

NEIL DEGRASSE TYSON: Esteller wanted to see if the twins' epigenomes might account for their differences. To find out, he and his team collected cells from 40 pairs of identical twins, age three to 74, then began the laborious process of dissolving the cells until all that was left were wispy strands of DNA, the master molecule that contains our genes.

Next, researchers amplified fragments of the DNA, until the genes themselves became detectable. Those that had been turned off epigenetically appear as dark pink bands on the gel. Now, notice what happens when the genes from a pair of twins are cut out and overlapped.

The results are far from subtle, especially when you compare the epigenomes of two sets of twins that differ in age. Here, on the left, is the overlapped DNA of six-year-old Javier and Carlos. The yellow indicates where their gene expression is identical.

On the right, is the DNA of 66-year-old Ana Mari and Clotilde. In contrast to the younger twins, hardly any yellow shines through. Their epigenomes have changed dramatically.

The study suggests that, as twins age, epigenetic differences accumulate, especially when their lifestyles differ.

MANEL ESTELLER: One of the main findings of our research is that epigenomes can change in function of what we eat, of what we smoke, of what we drink. And this is one of the key differences between epigenetics and genetics.

NEIL DEGRASSE TYSON: As the chemical tags that control our genes change, cells can become abnormal, triggering diseases like cancer. Take a disorder like MDS, cancer of the blood and bone marrow. It's not a diagnosis you'd ever want to hear.

SANDRA SHELBY: When I went in, he started patting my hand, and he was going, "Your blood work does not look very good at all," and that I had MDS leukemia, and that there was not a cure for it. And, basically, I had six months to live.

NEIL DEGRASSE TYSON: Was epigenetics the reason? Could the silencing of critical genes turn normal cells into cancerous ones? It's scary to think that a few misplaced tags can kill you. But it's also good news, because we've traditionally viewed cancer as a disease stemming solely from broken genes. And it's a lot harder to fix damaged genes than to rearrange epigenetic tags. In fact, we already have a few drugs that will work. Recently, Sandra Shelby and Roy Cantwell participated in one of the first clinical trials using epigenetic therapy.

JEAN PIERRE ISSA (M.D. Anderson Cancer Center): The idea of epigenetic therapy is to stay away from killing the cell. Rather, what we are trying to do is diplomacy, trying to change the instructions of the cancer cells, reminding the cell, "Hey, you're a human cell. You shouldn't be behaving this way." And we try to do that by reactivating genes.

SANDRA SHELBY: The results have been incredible, and I didn't have really any horrible side effects.

ROY CANTWELL: I am in remission. And going in the plus direction is a whole lot better than the minus direction.

NEIL DEGRASSE TYSON: In fact, half the patients in the trial are now in remission. But, while it maybe easier to fix our epigenome than our genome, messing it up is easier, too.

RANDY JIRTLE: We've got to get people thinking more about what they do. They have a responsibility for their epigenome. Their genome they inherit. But their epigenome, they potentially can alter, and particularly that of their children. And that brings in responsibility, but it also brings in hope. You're not necessarily stuck with this. You can alter this.

A Tale of Two Mice & Epigenetics

Name _____ Date _____

**View the audio slide show, "A Tale of Two Mice" (approximately 5 minutes)*

The Agouti gene in the yellow, obese mouse is methylated and shut down. In the brown mouse, about half of its cells are unmethylated, therefore, half of its genes turned off. What is the overall impact of DNA methylation on the mice?

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

Fill in the guided student worksheet below as you view the video, "Epigenetics":

1. Two people start out the same but their appearance and health can _____.

2. Epigenetics literally translates into just meaning _____ _____

_____.

3. It seems to me, this has profound implications for our _____.

4. So, who is your perfect lab human? _____ _____.

5. To find out, he and his team collected cells from _____ pairs of identical twins, ages three

to seventy-four.

6. One of the main findings of our research is that epigenomes can change in function of what we

_____, of what we _____, of what we _____.

7. Was epigenetics the reason? Could the silencing of critical genes turn normal cells into

_____ ones?

8. The idea of epigenetic therapy is to stay away from _____ the cell.

9. In fact, half of the patients in the trial are now in _____.

10. You're not necessarily stuck with this. You can _____ this.

TEACHER PAGES: ANSWER KEY FOR STUDENT WORKSHEET

A Tale of Two Mice & Epigenetics

Name _____ Date _____

View the audio slide show, "A Tale of Two Mice" (approximately 5 minutes)

The Agouti gene in the yellow, obese mouse is methylated and shut down. In the brown mouse, about half of its cells are unmethylated, therefore, half of its genes turned off. What is the overall impact of DNA methylation on the mice?

DNA methylation seems to have a negative impact on the health of the mice.

The yellow mouse exhibits a methylated Agouti gene which is not only affecting her coat color, but seems to be contributing to her tendency for obesity. The obesity then seems to be a contributing factor to her being at high risk for diabetes and cancer.

The brown mouse has half of the methylation and half of the turned off genes as compared to the yellow mouse. This mouse appears to be normal weight with a darker coat color.

In the case of these mice, more methylated DNA seems to correlate to greater health risk. In addition to impacting coat color, the Agouti gene, seems to be an indicator of health in these mice as well.

Much more research will need to be done to give us a clearer understanding of the health consequences of methylated vs. non-methylated DNA on specific genes.

Fill in this guided student worksheet as you view the video, "Epigenetics":

1. Two people start out the same but their appearance and health can diverge .

2. Epigenetics literally translates into just meaning above the genome.

3. It seems to me, this has profound implications for our health.

4. So, who is your perfect lab human? identical twins.

5. To find out, he and his team collected cells from 40 pairs of identical twins, ages three to seventy-four.

6. One of the main findings of our research is that epigenomes can change in function of what we eat , of what we smoke , of what we drink .

7. Was epigenetics the reason? Could the silencing of critical genes turn normal cells into cancerous ones?

8. The idea of epigenetic therapy is to stay away from killing the cell.

9. In fact, half of the patients in the trial are now in remission .

10. You're not necessarily stuck with this. You can alter this.

LESSON THREE: "SCIENCE TAKE-OUT: GENE SWITCHES"

KEY QUESTION(S): How and why do genes turn "off" and "on"? What can we learn from modeling an operon?

OVERALL TIME ESTIMATE:

- Advance Preparation: 15 minutes (5 minutes to set up lab stations with Science Take-Out kits; 10 minutes to make copies of student lab questions/worksheets)
- Student Procedure: one 40- 50 minute class period

LEARNING STYLES: Visual and kinesthetic

VOCABULARY:

Transcription: DNA to RNA; during a transcription, a DNA sequence is read by an RNA polymerase, which produces a complementary, antiparallel RNA strand. The RNA complement includes Uracil (U) is all instances in which Thymine (T) would have occurred in a DNA complement.

Gene: Unit of heredity existing as alleles on the chromosomes; typically, two alleles are inherited, one from each parent.

Operon: Group of structural and regulating genes that function as a single unit.

lac Operon: Operon required for the transport and metabolism of lactose in E. coli and other bacteria. The lac operon allows for the effective digestion of lactose when glucose is not available.

trp Operon: A group of genes that are used, or transcribed, together — that codes for the components for production of tryptophan. The trp operon is present in many bacteria, but was first characterized in E. coli.

Regulator Gene: Gene that controls the expression of another gene(s); in an operon, regulator genes code for repressor proteins.

Promoter: In an operon, a sequence of DNA where RNA polymerase binds prior to transcription.

Repressor Protein: In an operon, protein molecule that binds to an operator, preventing transcription of structural genes.

LESSON SUMMARY:

Gene activity influences phenotypic expression. In this collaborative investigation, students will explore how bacteria may turn genes off or on. Students will model a gene switch in bacteria and the action of an operon that regulates gene expression. This two-part modeling exercise uses a variety of hands-on manipulatives to assist students in visualizing the gene switch concept. A teacher-led discussion will explain how gene switches may occur due to transcription factors or epigenetic influence.

STUDENT LEARNING OBJECTIVES: The student will be able to……

14. Describe differences and similarities between lac and trp operons.
15. Explain how genes may switch off and on.
16. Describe how gene regulation impacts phenotypic expression.

STANDARDS:

Florida Standards: SC.912.L.14.6

SC.912.L.15.15

SC.912.L.16.3

SC.912.L.16.4

SC.912.L.16.5

SC.912.L.18.4

SC.912.L.18.11

SC.912.N.1.1

SC.912.N.1.6

SC.912.N.1.7

AP Biology 3.A.1 (LO 3.1-3.6)

3.B.1 (LO 3.18-3.21)

3.B.2 (LO 3.22-3.23)

MATERIALS:

- Science Take-Out "Gene Switches" kit; one per lab group, student pair, or individual http://www.sciencetakeout.com/wp-content/uploads/2014/10/TEACHER-ONLINE-Gene-Switches-9-27-14.pdf, #STO-143

Purchase Information:	Quantity	Price
	1-9	$10.00 each
	10-24	$9.50 each
	25-1000	$9.00 each

BACKGROUND INFORMATION

How do bacteria turn on and turn off genes? Students model the action of the lac operon that regulates the expression of genes essential for lactose metabolism.
Core Concepts:
- Switching genes on and off enables bacteria to conserve resources by producing proteins only when they are needed.
- Operons are genetic control units that are turned off when a repressor protein combines with an operator.
- Lactose molecules may act as inducers that turn on inducible operons by deactivating repressor proteins.

ADVANCE PREPARATION:

1. Purchase Science Take-Out, "Gene Switches" Kit
2. Use preparation guide in the Science Take-Out kit.
3. Copy student pages from Science Take-Out kit for each student; students will need pages to respond to the questions accompanying the activity.

PROCEDURE AND DISCUSSION QUESTIONS WITH TIME ESTIMATES:

9. (40 minutes) – Have students work in pairs to follow the directions provided.

(This procedure could be altered to one kit per student, or one kit per small group.)

ASSESSMENT SUGGESTIONS:

- Student worksheet may be graded for accuracy or completion as a class work grade.

EXTENSIONS:

Optional Extension - In the trp operon, the repressor protein is usually inactive, allowing the transcription of structural genes necessary for the production of the amino acid tryptophan. When tryptophan is present in the environment, bacteria no longer need to produce their own tryptophan. Tryptophan acts as a repressor signal by binding to and activating the repressor protein. The repressor protein then binds to the operator.

1. Use the kit pieces and the information above to model how a trp operon turns off the production of tryptophan when tryptophan is present. You may use additional parts if you wish. Draw and label your model in the space below.

2. Make a T chart to compare and contrast the lac and trp operons. Lac Operon—an inducible operon, Trp Operon—a repressible operon - Describe differences and similarities.

RESOURCES/REFERENCES:

1. http://www.hhmi.org/biointeractive/gene-switch, ***Gene Switch***, part of *Evolution: Constant Change and Common Threads*; downloadable animation.
Summary: Regulatory "switches" are found upstream from a gene. Regulatory molecules bind to the switches and recruit RNA polymerase to bind to the gene's promoter region, increasing the transcription of the gene into messenger RNA.

2. http://www.ncbi.nlm.nih.gov/books/NBK26872/, ***How Gene Switches Work***, from Microbiology of the Cell. 4th Edition. New York, Garland Science, 2002.

3. http://www.pbs.org/wgbh/nova/body/gene-switches.html, ***Gene Switches***, NOVA, PBS, by Nipam Patel, August 1, 2007. (slide show)

4. http://science.howstuffworks.com/life/genetic/genes-turned-off-on.htm, ***How are Genes Turned Off and On***, How Stuff Works, by Elizabeth Sprouse.

TEACHER PAGES: SCIENCE TAKE-OUT, "GENE SWITCHES" STUDENT HANDOUT (SAMPLE)

STO-143

Gene Switches

Teacher Information

science take-out
just add students

Summary

How do bacteria turn on and turn off genes? Students model the action of the lac operon that regulates the expression of genes essential for lactose metabolism.

Core Concepts

- Switching genes on and off enables bacteria to conserve resources by producing proteins only when they are needed.
- Operons are genetic control units that are turned off when a repressor protein combines with an operator.
- Lactose molecules may act as inducers that turn on inducible operons by deactivating repressor proteins.

Time Required

One 40-minute class period

Kit contains

- Large straw pieces (genes in an operon)
- Chenille stem
- Mini hair clip (repressor protein)
- Labels for parts of the operon
- Plastic car (RNA polymerase)
- Twist tie (messenger RNA)
- Beads (ribosomes)
- Plastic sword, ring, and cube (enzymes)

Reusing the kit

All parts of kit can be reused. Instruct students to save all materials.

Warning: Choking Hazard
This Science Take-Out kit contains small parts. Do not allow children under the age of seven to have access to any kit components.

LESSON FOUR: DETECTING EPIGENETIC DNA METHYLATION IN ARABIDOPSIS

KEY QUESTION(S): Can a methylation-dependent restriction enzyme, McrBC, be used as a diagnostic tool for studying gene regulation in Arabidopsis thaliana?

OVERALL TIME ESTIMATE:

- Advance Preparation: 15 minutes (5 minutes to set up lab stations with Science Take-Out kits; 10 minutes to make copies of student lab questions/worksheets)
- Student Procedure: one 40- 50 minute class period

LEARNING STYLES: Visual and kinesthetic

VOCABULARY:
DNA Methylation: process by which methyl groups ($-CH_3$) are added to nuclear DNA; attach to cytosine.

Homeotic Gene: regulates the development of anatomical structures in various organisms such as insects, mammals, and plants.

Flowering Wageningen (FWA): a homeotic gene that controls flowering time, normally expressed in endosperm.

Homeotic Mutation: one part of an organism is transformed into another.

Polymerase Chain Reaction (PCR): technique used to amplify quantities of DNA.

LESSON SUMMARY:
Students will prepare for this activity weeks in advance due to the need for flowering *Arabidopsis thaliana* plants. Phenotypic variance will be observed in the plants. Further investigation will include DNA extraction, restriction enzyme digest, PCR, gel electrophoresis, and bioinformatics to investigate the role of DNA methylation in gene regulation. Students will work in collaborative groups to follow protocol and complete the laboratory assessment.

ARABIDOPSIS seed will be grown in class. Students can easily observe that wild-type FWA plants flower several weeks earlier than FWA mutants, which also develop much larger leaves. DNA extracted from both types of plants will then be incubated with a methylation-dependent restriction enzyme called McrBC, which cuts DNA within heavily methylated regions. Wild-type FWADNA is methylated, and so is cut by McrBC. DNA from the FWA mutant is uncut. Then add primers spanning the FWA promoter to both types of DNA and the region will be amplified by polymerase chain reaction (PCR). Agarose gel electrophoresis will show that DNA from the uncut FWA mutant DNA amplifies to produce a band of the predicted size; however, the cleaved wild-type DNA fails to amplify and produces no visible band.

This experiment offers a sophisticated test for specific chemical changes to DNA that act as an important developmental regulator in plants. Recent advances in technology now allow scientists to view the "epigenome," or complete set of epigenetic modifications for the genome of any species. We are beginning to understand more and more about how these epigenetic changes operate "above" the genome to control development and contribute to human health. Errors in epigenetic modification contribute to more than 70 human diseases, including many forms of cancer.

STUDENT LEARNING OBJECTIVES: The student will be able to……

17. Explain the process of epigenetic modification of a genome.
18. Describe the role of DNA methylation in gene expression.
19. Describe phenotypic differences in flowering of Arabidopsis plants.
20. Explain how DNA extraction, restriction enzyme digest, PCR and gel electrophoresis procedures are used for DNA analysis.

STANDARDS:

Florida Standards: SC.912.L.14.6

SC.912.L.15.15

SC.912.L.16.3

SC.912.L.16.4

SC.912.L.16.5

SC.912.L.18.4

SC.912.L.18.11

SC.912.N.1.1

SC.912.N.1.6

SC.912.N.1.7

AP Biology 3.A.1 (LO 3.1-3.6)

3.B.1 (LO 3.18-3.21)

3.B.2 (LO 3.22-3.23)

MATERIALS:

Components	Qty
Arabidopsis **Seed Pack from** ***Ler*** **(Landsberg** ***erecta*****) Wild Type** ♦	1
Arabidopsis **Seed Pack from** ***fwa-1*** **(*flowering wageningen*) Mutant** ♦	1
Planting Flat and Tray	1
Plastic Dome Lid	1
Potting Soil, Bag ♦	1

Nuclei Lysis Solution, 12 mL	1
RNAse Solution, 5 mg/mL, 250 µL ♦	1
Protein Precipitation Solution, 3.5 mL	1
Isopropanol, 100%, 20 mL	2
Ethanol, 70%, 30 mL	1
DNA Rehydration Buffer, 2.5 mL	1
***FWA* Primer/Loading Dye Mix, 700 µL** ♦	1
Plastic Pestles	15
Ready-to-Go™ PCR Beads, 0.2-mL Tubes	25
pBR322/*Bst*NI Markers, 0.075 µg/µL, 130 µL ♦	1
McrBc Buffer, 10×, 200 µL ♦	1
Sterile Distilled Water, 1 mL ♦	1
McrBc Enzyme, 10 U/µL, 20 µL ♦	1
Guanosine 5′–Triphosphate (GTP), 100 mM, 15 µL ♦	1
BSA, 10 mg/mL, 30 µL ♦	1
Mineral Oil, 5 mL	1
Teacher's Manual with Reproducible Student Guide	1
Tweezers, Scissors, or Scalpel	
Water Baths/Heating Blocks (65° C and 37° C)	

Micropipets and Tips, 1 to 1,000 µL	
Microcentrifuge	
Microcentrifuge Tubes, 1.5 mL	32
Microcentrifuge Tube Racks	8
Thermal Cycler, Programmable	1
Electrophoresis Chambers	
Electrophoresis Power Supplies	
Vortexer (optional)	
Container with Ice	
Computer with Internet Access	
Microwave, Hot Plate, or Boiling Water	

BACKGROUND INFORMATION

Arabidopsis thaliana is an annual plant that usually grows about 20–25 cm tall. The leaves form a rosette at the base of the plant, with a few leaves also on the flowering stem. The basal leaves are green to slightly purplish in color, 1.5–5 cm long and 2–10 mm broad, with an entire to coarsely serrated margin; the stem leaves are smaller. Leaves are covered with small, unicellular hairs called trichomes. The flowers are 3 mm in diameter, arranged in a corymb; their structure is that of the typical *Brassicaceae*. The fruit is a siliqua 5–20 mm long, containing 20–30 seeds. Roots are simple in structure, with a single primary root that grows vertically downward, later producing smaller lateral roots.

Arabidopsis can complete its entire lifecycle in six weeks. The central stem that produces flowers grows after about three weeks, and the flowers naturally self-pollinate. In the lab, *Arabidopsis* may be grown in Petri plates, pots, or hydroponics, under fluorescent lights or in a greenhouse. The small size of its genome, and the fact that it is diploid, makes *Arabidopsis thaliana* useful for genetic mapping and sequencing — with about 135 mega base pairs and five chromosomes, *Arabidopsis* has one of the smallest genomes among plants.

ADVANCE PREPARATION:

4. Purchase *"Detecting Epigenetic DNA Methylation in Arabidopsis Amplification Kit*", item # 211403 from Carolina Biological Supply Company, $285, available after August 2, 2016.

5. Plant *Arabidopsis* seeds at least five weeks before experimentation date. Mature plants will be needed for DNA extraction.

6. Copy student pages from kit for each student; students will need pages to respond to the questions accompanying the activity.

PROCEDURE AND DISCUSSION QUESTIONS WITH TIME ESTIMATES:

10. (40 minutes) – Have students work in pairs to follow the directions provided.

    (This procedure could be altered to one kit per student, or one kit per small group.)

ASSESSMENT SUGGESTIONS:

- Student worksheet may be graded for accuracy or completion as a class work grade.

EXTENSIONS:

RESOURCES/REFERENCES:

5. http://www.hhmi.org/biointeractive/gene-switch, ***Gene Switch***, part of *Evolution: Constant Change and Common Threads*; downloadable animation.

Summary: Regulatory "switches" are found upstream from a gene. Regulatory molecules bind to the switches and recruit RNA polymerase to bind to the gene's promoter region, increasing the transcription of the gene into messenger RNA.

6. http://www.ncbi.nlm.nih.gov/books/NBK26872/, ***How Gene Switches Work***, from Microbiology of the Cell. 4th Edition. New York, Garland Science, 2002.

7. http://www.pbs.org/wgbh/nova/body/gene-switches.html, ***Gene Switches***, NOVA, PBS, by Nipam Patel, August 1, 2007. (slide show)

8. http://science.howstuffworks.com/life/genetic/genes-turned-off-on.htm, ***How are Genes Turned Off and On***, How Stuff Works, by Elizabeth Sprouse.

TEACHER PAGES: LAB SHEETS NOT AVAILABLE UNTIL 8/2/2016

ASSESSMENT

Assessments for ***Epigenetics: MZ Twin Studies***

1. Students will read article "*Same But Different – How epigenetics can blur the line between nature and nurture*", by Siddhartha Mukherjee (2011 Pulitzer Prize winning author). The assessment for the article will include ten multiple choice and ten short answer questions.

2. Science Take Out Activity – *Gene Switches*. The assessment for this activity will consist of 25 short answer questions regarding procedural steps in the investigation that test knowledge of the concepts behind the activity which include lac and trp operons and mutations.

3. "Gene Switches" is a slide show tutorial produced by NOVA, http://www.pbs.org/wgbh/nova/genes/ , the assessment will consist of 10 multiple choice questions that address the content of the tutorial.

4. Lab Assessment – Laboratory Write-up in class lab notebook in addition to completed lab sheets provided by Carolina Biological Supply to accompany the lab "*Detecting Epigenetic DNA Methylation in Arabidopsis Kit*", http://www.carolina.com/dna-learning-center-dnalc/detecting-epigenetic-dna-methylation-in-arabidopsis-kit/FAM_211403.pr