**Title:** The Science and Ethics of Biotechnology

**Length of Course:** 1 year/2 semesters

**Subject Area and Discipline:** Laboratory Science ("d") - Interdisciplinary Science

**UC Honors Designation:** Honors

**CTE Sector:** Health Science and Medical Technology

**CTE Pathway:** Biotechnology

**Grade Level(s):** 11-12

**Prerequisites:** Algebra 1, Biology

**Recommended Prerequisites:** Chemistry, Algebra 2

---

## Course Overview:

Modern biological and laboratory techniques have opened a wide range of topics and opportunities for secondary students to explore and experience. With the goal of building understanding and mastering essential laboratory techniques, students examine concepts and conduct relevant and authentic laboratory investigations. Students review and extend learning in cell biology, biomolecules and atomic structure, DNA, gene expression and genetic code, evolution, physiology, and energy and metabolism. Students apply this knowledge to the learning and practice of lab techniques used in academic, commercial, and medical laboratories, such as PCR, electrophoresis, transformation, and cell culturing and generate authentic and relevant products similar to those created and interpreted in any number of labs applying biotechnology. Additionally students explore ways to communicate scientific information and ultimately produce a report in the form of a scientific journal article. A key aspect of this course is the examination of where ethics and biotechnological approaches intersect, and in each unit, students confront an ethical question related to the unit content and techniques. Ultimately, this course aims to produce technically sound scientists who are able to evaluate information and make informed decisions, especially when larger ethical conflicts may be involved.

## Course Content:

### Unit 1: Overview of Biotechnology (Marine Biotechnology/ Environmental/ Bioremediation/ Plant)

This unit will immerse students in an environment that is similar to the research environment of a biotechnology company. They will experience the steps required to produce a biofuel by utilizing good laboratory practices, lab protocols, and scientific inquiry. An important element of creating any new product in biotechnology is "selling" the idea to industry. Students will learn how to develop an authentic business model which outlines the necessary production steps and conforms to good manufacturing practices (GMPs) for producing their biofuel. Students will also explore possible careers in the industry and will learn the laws that regulate pharmaceutical manufacturing.

### Unit 1: Key Assignments

#### 1: Biofuel Production Lab

The biofuel production lab is an introductory lab to hook students into the field of Biotechnology. In this lab, students will first convert cellulosic biomass sources into glucose and then into ethanol. Students will work collaboratively to research different types of cellulosic biomasses and choose one which they believe would be an effective substrate. Students need to be able to justify their selection and develop a business model explaining how they will obtain large quantities of the cellulosic biomass. Before the experiments begin, students will present their proposal via multimedia presentation just as if they were working in industry. Students will then spend several class periods carrying out their experiments. They will be responsible for designing their positive and negative controls and propose any extra experiments that would be helpful to collect specific to their substrate. The lab protocol is meant to be open ended which gives students the flexibility to optimize their experimental procedures. Students will measure the concentration of glucose either using a colorimetric assay or glucose meter and the concentration of ethanol using an ethanol probe. At the end of experiment, students will continue to work in their lab groups as they analyze their data and draw conclusions of the effectiveness of their substrate. Students will then present their work by typing a formal lab report in the form of the materials and methods and results section of a scientific journal article. These reports can be shared with the class and evaluated by the instructor.

#### 2: Research Careers

In order to explore potential careers in the bioscience and biotechnology fields, students will work in small groups to research one type of position. Students can use many online sites for this research such as:

http://www.ultimatestaffing.com/
https://orangecounty.craigslist.org/search/sci
https://www.usajobs.gov/
http://www.ambrygen.com/careers
http://www.zymoresearch.com/careers
http://www.bausch.com/our-company/careers#.V-cdsfArL4c
http://www.abbottmedicaloptics.com/about-amo/careers
https://jobs.jnj.com/jobs?page=1&keywords=technician
https://theapplicantmanager.com/careers?co=ro
http://wcct.com/contact-us/clinical-research-careers/
http://www.irvinesci.com/about-us/careers
http://www.asmcareerconnections.org/
http://abe-la.org/uploads/3/4/8/3/34833906/careersinbiotechbooklet3ed.pdf

Students will collect data on job title, salary, education required, skills required, experience required, job outlook, examples of companies offering this type of position, job duties and responsibilities, pros and cons. Each group will put this information together into a job profile.The class will utilize the job profiles to assemble a classroom book on Careers in the Biosciences.

### 3: FDA Computer Activity

The Code of Federal Regulations (CFR) is a list of general and permanent rules of the United States government. These regulations are enforced by the federal agencies, such as the FDA. In this computer activity students will explore the federal regulations pertaining to pharmaceutical manufacturing. Students will be introduced to the laws, learn how to read a CFR and how to access them on the internet. The sections of the GMP regulations will be divided so that all sections of the regulations have been covered within a class. Students will work in groups to research sections of the GMP regulations assigned to them. They will then prepare a bullet point summary of their findings. Next, groups present their findings to the class using a multimedia presentation. Their presentation will include identification of the points that require a list of procedures and a record of the scientists' experiments. After all of the groups have presented their findings, students will individually write a summary of how GMP regulations fit together and serve as the foundation of a quality system for a laboratory in a pharmaceutical company.

## Unit 2: Cell Biology (Medical/ Biopharmacy)

This unit integrates acquired knowledge about cell structure with information regarding the differences in the requirements and conditions needed to grow different types of cells used in research, product, and biopharmaceutical production. Additionally, students investigate the advantages and limitations of using specific cells in place of whole mammalian systems to test the effects of molecules. Within this unit, the commonly used method of employing the spectrophotometer to determine cell density is introduced. Students will learn and apply Current Good Laboratory Practices for laboratory quality control (cGLP), proper laboratory documentation, the Global Harmonizing System for laboratory safety including sample storage (GHS), Standard Operating Procedures (SOPs) and use of laboratory instruments. After growing eukaryotic algae on various substrates to produce a biofuel in the previous unit, the students are introduced to the differences between eukaryotic and prokaryotic cells including differences in DNA, and the practice of employing various cell types, such as mammalian, yeast, insects, or bacteria for production of various types of products. Finally, students will explore the advantages and limitations of cell culture which necessitates the use of whole animal models.

## Unit 2: Key Assignments

### 1: Growth/ Culture Lab

Students will compare the growth of yeast or prokaryotic cells under various growth conditions. Students will use aseptic technique, cGLP standards with proper liquid handling to measure the concentration of cells at specific times using a spectrophotometer. After collecting data, they will generate a graph of the growth curve and determine the best condition to grow that type of cell. Throughout the lab, students will document their protocol, results, calculations and conclusions in their scientific notebook. A scientific report in the form of the materials and methods and a results section of a scientific journal article will be shared with the class and evaluated by the instructor.

### 2: The Ethical Considerations Concerning Animal Use in Biomedical Research

Building upon the knowledge acquired in this unit regarding the use of various cell types to produce desired products, students will research the application of cell lines for the purpose of research in the biomedical field. They will specifically investigate the advantages and shortcomings of using cell lines and then determine what purpose animal models serve. Additionally, they will determine the implications for biomedical investigations when taking a position for the continued or discontinued use of animals. Using the results of their investigation and knowledge gained from assignment one, students will form groups and produce a one-minute public service announcement

advocating for or discouraging the continued use of animals for biomedical investigations. This assignment reinforces the concept that biotechnology affects biomedical advances and that educated and informed individuals may have differences in beliefs despite possessing similar depth of knowledge.

## Unit 3: Bio-molecules and Atomic structure (Biopharmacy/Medical Biotech

Whether a lab technician works the area of Biopharmacy or Medical Biotechnology, he or she has to have a strong foundation in biochemistry and technically sound laboratory skills. In this unit students will review the basic building blocks of matter, starting with the atom and culminating with the study of the biomolecules structures and function. Students will also focus on laboratory skills necessary for any job in industry, regardless of the focus. The laboratory skills learned in this unit include how to accurately use equipment commonly found in industry, such as micropipettors, volumetric pipettes, balances, and spectrophotometers. Students will also learn how to prepare solutions which is the first step in any of the labs in the subsequent units. Lastly, students will be introduced to experimental design and carry out a colorimetric assay using the spectrophotometer. Again, this serves as a foundational lab technique that can be used to determine concentration or monitor enzymatic activity in future units. As students learn these lab techniques, they will explore the industry standard for each and the consequences for performing below these standards. Students then apply their understanding of industry standards and quality of results to what it takes for a Medical biotechnology company to bring a potential drug through the product pipeline and the ethical challenges a company might face.

## Unit 3: Key Assignments

### 1: Four Levels of Protein Structure Tutorial

Students will interactively explore the 3D structure of a protein using a tutorial such as *Four Levels of Protein Structure* (see URL below). During the tutorial students will take snap shots (pictures) of their manipulated and labeled protein structures showing primary, secondary, tertiary and quaternary structures. Students will collect their snapshots and organize them in a multimedia presentation to present to the class.
http://workbench.concord.org/database/activities/322.html

### 2: Solution Preparation via Dilution and Spectrophotometer Lab

In this activity, students learn the foundational laboratory skills needed to prepare solutions, and learn to use laboratory equipment such as pipetman, volumetric pipettes, and spectrophotometers. First students will work in teams to design their procedures for the preparation of five known standard solutions. They will make a stock solution followed by a series of dilutions. Once their standard solutions are made they will use

the spectrophotometer to measure the absorbance and create a standard curve. Students will then be given an unknown solution and use their standard curve to determine its concentration. Students document all the procedures and calculations in their lab notebook. In their report, they will include a computer generated standard curve and a discussion of the quality of their results based on an assessment of their $R^2$ value. These should be shared with the class to facilitate later discussions in assignment 4.

### 3: Using the Bradford Assay to Analyze Protein Content in Common Foods Lab

Determining an unknown by comparing to known standards is a foundational skill for the laboratory. Students will use the skills obtained in assignment #2 lab to determine the protein content in different types of milk and compare it to protein content published on the nutrition labels. In order to determine the concentration of protein in milk, students must first prepare a series of known solutions of BSA and perform a Bradford assay. They will then report their absorbances in their lab notebook. Using computer software, students will generate a standard curve. Students will then perform a Bradford assay on their milk samples and use their standard curves to calculate the concentration of protein. After collecting data, students will then write a report in the format of a results section, with an appropriately formatted graph, to mimic that of a journal publication. These will be shared with the class to facilitate later discussions in assignment 4 and evaluated by the instructor.

### 4: Ethics: Kelsey Case Study.

In assignments 1-3, students learned techniques used to analyze the quality and quantity of a product in development by a biotech company (measurement taking, the variability of collected data amongst groups performing the same tasks, and the lab skills that would be used in a medical biotechnology company) which directly relates to larger studies dealing with products that impact human health. Using their new insights into data collection and determining quality of data learned in this unit, students analyze a case study and make a recommendation to the FDA Re: whether the given drug (thalidomide) should be pushed through the product pipeline. Students explore the 1960s case in which Dr. Kelsey and her colleagues at the FDA took a conservative route and did not allow thalidomide to be distributed for public use. This was a different approach compared to Germany's decision to move forward with the drug. Student recommendations should consider the following questions: How does society balance the potential benefit of new pharmaceuticals against their potential risk? And what are the responsibilities of companies to ensure the safety of drugs? Once students have researched the process by which a drug goes through to be approved by FDA and examined both the United States and Germany's approaches to helping their patients,

they will engage in an optional class debate where they will have to defend their recommendations.

## Unit 4: DNA Molecule (Agricultural Biology/ Animals/ Food)

In this unit, students apply their knowledge of the cell from unit 2 and their understanding of biomolecules from unit 3 to explore the replication and structure of DNA. Students will use plasmid DNA to transform bacterial cells to visualize how the transfer of genetic material directly impacts an organism and to perform the same techniques actively used by the biotechnology industry. Students further explore biomolecule structure in assignments 2 & 3 and work with enzymes to manipulate DNA and visualize it using gel electrophoresis. These techniques and assignments introduce students to the concepts of DNA sequence, genes, and the mathematical determination of efficiency in the laboratory. This basic understanding of DNA and enzyme biomolecules will be necessary for the students understanding of the material in Unit 5. After completing assignments 1-3, students get a feel for how easy it is to manipulate DNA. Assignments 4 & 5 will explore how different industries use these concepts in the manipulation of DNA and the ethical consideration of these techniques.

## Unit 4: Key Assignments

### 1: Transformation of plasmid DNA into E.coli Lab

In this activity, students will learn a foundational skill in genetic engineering: how genes from one organism can be introduced into another organism using the process of transformation. Students will be given plasmid DNA containing a selectable marker and the gene for green fluorescent protein (GFP). Students will grow bacterial cultures and prepare them for transformation using calcium chloride. Students will transform the bacteria with the plasmid DNA and select for transformed organisms using media plates with the appropriate antibiotic. Plates will be inspected to see if they contain transformed bacteria. In order to show students that competency in the lab can be quantitatively evaluated by industry and others, the efficiency of their transformation process will be assessed mathematically. Each student will calculate the number of colonies observed versus the quantity of plasmid DNA used in the transformation process. This data along with the experimental procedure will be reported in their laboratory notebook. The class will discuss the concept that the laboratory notebook is a legal document in industry and the importance of accurate documentation of all steps, observations, and outcomes of experiments.

### 2: Restriction Digest Analysis of DNA Lab

After performing the procedures to introduce new DNA into an organism in assignment 1, students will explore how that same DNA can be manipulated by another biomolecule

- enzymes. Students will grow their transformed bacteria and isolate plasmid DNA from the bacteria using the alkaline lysis method or a DNA isolation kit (ie. from Zymo Research). Students will learn how to read a plasmid map by completing a worksheet. Based on their map interpretation they will select restriction enzymes and predict cleavage fragments from a restriction enzyme digest. Students will produce a plasmid map of their predicted fragments. The students will then digest their plasmid DNA with the restriction enzymes. Student will use their isolated DNA for the next assignment and keep their plasmid maps to compare to their final results.

**3: Agarose Gel Electrophoresis Lab**

In order to analyze their restriction digest results, students will run their digested DNA on an agarose gel. Students will load the gel with their samples and with a DNA ladder and then separate the DNA fragments using gel electrophoresis. Following this lab students will analyze their data from the gel electrophoresis and determine if they obtained DNA fragments of their predicted size. Students will be required to present their results using their scientific data in a poster or a multi-media presentation and include a description supporting why they did or did not obtain their predicted results.

**4: Biotechnology Connection: Cloning/ Genetic Engineering**

Now that students have had the opportunity to explore and experience the methods of genetic engineering by manipulating DNA in assignments 1-3, they discuss how these powerful techniques can be used by industry and the ethical implications of these applications and other advanced techniques of genetic engineering, including whole organism cloning. After discussing applications of genetic engineering, the different types of cloning and debating the ethical issues involved in each type of cloning, the class will use the democratic process to suggest "cloning laws" and will vote on which "laws" will be instituted in their "country". Students will make posters outlining the new laws and develop a press release supporting their new laws.

Other Cloning Resources:

https://www.tes.com/resources/search/?&years=US%7C0%7C9th%7C&years=US%7C0%7C10th%7C&years=US%7C0%7C11th%7C&years=US%7C0%7C12th%7C&subjects=US%7C0%7CBiology%7C&&displayCcountry=US&q=cloning

**#5: Ethics: GMO/ Patenting**

After gaining insight into DNA manipulations and the ethical arguments surrounding this activity achieved in assignments 1-4, students will further explore ethical considerations and industrial applications of genetic engineering by researching court cases regarding GMO plants and patented human genes. Students will work in groups to discuss the cases and analyze the good and bad aspects of each case and each participant in the

case. The group will orally present their cases to the class and outline their conclusions on culpability as well as the impact this case had on the community.

## Unit 5: Gene Expression and Genetic Code (Biomanufacturing/Medical)

Students will examine the central dogma of cell biology and put into practice the *in vitro* production and isolation of a protein product from *E. coli*. Students investigate the application of biomanufacturing in various fields as part of a research project, and also consider the ethical implications of using a human derived cell line, HeLa cells, for continued scientific and industrial research. Production of plastics, industrial enzymatic processes, medical treatments, and scientific research are a few examples of where protein production has become an essential technique. The application of biotechnology in biomanufacturing has lead to significant advances in research and industry. Students will model the large-scale process of biomanufacturing by producing and isolating protein product from bacterial cell culture during a wet lab. In a follow-up research assignment, the application of the biomanufacturing process will be investigated. Students will produce a comprehensive presentation taking the perspective of a biotech consulting company presenting to target audience. Finally, the ethical implications of continued use of the HeLa cell line for industrial and research purposes will be debated by students. The debate will take the form of a civil case with students filling the roles of justices, counselors, and expert witnesses.

## Unit 5: Key Assignments

### 1: Grow/Collect/Assess Protein Product (Lab)

Students will complete the process of bacterial transformation and expression of a protein product started in Unit 4. After transforming bacteria with an expression vector, students will grow and ultimately harvest protein product from bacterial cell (E. coli) culture. While any number of available kits (ex: Bio-Rad GFP) would be sufficient, it would be ideal that the model used be the same as used in Unit 4. In order to isolate protein, students will need to transform and plate bacteria, select colonies, grow colonies under antibiotic selection, and extract protein product from the bacteria. Students will then assess product for purity and quantity using a spectrophotometer and write up their results in a lab report. To increase rigor and bring in previously developed skills, various changes to the conditions could be introduced, including, but not limited to, temperature, time, and nutrient concentration. Students would then compare approaches based on the amount and purity of the protein product isolated. In addition to proper documentation in their laboratory notebooks, students will produce an abstract of their project as if they were submitting it for acceptance to a scientific conference. The completion of this lab activity will provide experience and context for the completion of the biomanufacturing research project (Assignment #2).

### 2: Biotechnology Connection - Biomanufacturing

Once students have conducted a protein isolation, they begin a research project examining the process and approaches used to biomanufacture various proteins. A key part of this research project will be expanding on the underlying mechanistic and biological bases and the advantages/disadvantages to utilizing various *in vivo* and *in vitro* processes to produce biological products. For example, students may decide to address the production of porcine insulin in bacterial culture for treatment of diabetes in humans. The focus of the research would be the purpose and decisions behind using the production process. Various elements should be addressed, including a description of the process, pros, cons, economic considerations, and biological efficacy. Students can present their findings as a "sales" pitch to a target audience, such as an industrial corporation looking to produce a biological molecule.

### 3: Ethics: Henrietta Lacks

Students read excerpts from The Immortal Life of Henrietta Lacks, or alternative publication/article, which discusses ethical dilemmas presented by the continued use of HeLa cells in numerous biotechnological applications. The primary ethical conflict, as students will discover in the reading, is that the cells were collected without the consent of either Henrietta Lacks or her surviving family. Some questions that should be considered by students include: Who owns the cell line? What rights are involved? Where does the greater good fit in? Students address the ethical conflict and the questions it creates in the model of a supreme court case, or similar forum. This mirrors a forum where ethical issues are addressed, discussed, and resolved and where students can verbally state their opinions and utilize their research and scientific knowledge in a range of roles (justices, counselors, expert witnesses, family members, etc.) to ensure all students have an opportunity to participate. The end product is a written paper that takes the form of a legal decision handed down by a justice (examples are easily available online) in response to the court case.

## Unit 6: Basic Mendelian Genetics

In this unit students will build on their knowledge of protein structure and DNA heredity by looking at two examples of genetics in medicine. They will explore the basic genetic concepts of genotype, phenotype, alleles, dominance, etc. by studying a gene allele that gives rise to cancer. The mutated gene causes a conformational change in the enzyme and students will explore the effect on protein function. Next, students will analyze human hair DNA for alleles of a specific sequence (such as Alu elements) to determine variability in the population. They will look at genetic testing used in cancer screening and the role of genetic counselors and patient information in making informed care

decisions. After this, students will evaluate the genetic tests available and will produce a folder in which test methods are outlined along with key characteristics of that test. Finally, they will explore the use of statistics as a tool for determining validity by understanding statistical significance.

## Unit 6: Key Assignments

### 1: Cancer as a Genetic Disease

In this assignment students utilize their knowledge of the structure of biomolecules to examine the gene alleles and proteins involved in cancer arising from a BCR-ABL kinase mutation. Students begin by reviewing basic Mendelian genetics and analyze pedigrees to look for disease patterns. Students will analyze the phenotypic and genotypic occurrence of the mutated gene. Students work in small groups to examine what happens to the protein that contains the mutation and how genetic mutation leads to a conformational change, which thus interrupts cellular processes within the cell. Students work with molecular models to visualize the effect a genetic mutation may have on a functional protein, and produce two flow diagrams, one that outlines the steps involved in the normal functioning of the kinase and one that outlines the steps involved in the functioning of the mutant kinase found in a person with this form of cancer. The diagram should clearly indicate where normal functioning of the kinase stops. Students will use their diagrams to predict the outcomes of this breakdown in function, including symptoms observed in a patient and include this in their lab report.

### 2: It's as Easy as Pulling Hair - Bio-Links Activity and Lab

This assignment introduces students to a case study on the genetic testing of an individual for brain cancer. Students begin with the laboratory portion of the assignment, in which they process their own DNA (their hair) as the sample to look for genetic markers using the following techniques: Isolation of DNA from Hair, PCR Amplification of a Human DNA sequence such as Alu, Restriction Digest Analysis, and Gel Electrophoresis. Students analyze human DNA from a strand of hair and then use their resulting data to construct a larger DNA population frequency database based on the alleles they identified in their class data. This part of the assignment introduces students to the process of genetic testing and will help them determine where procedures can go wrong or provide false results. The class should work together to create a list of problems that can arise with the data collection and analysis from this type of test procedure.

Part two involves the human impact of genetic testing. In a case study such as "Easy as Pulling Hair Activity," (www.bio-link.org/home2/sites/files/pullinghairstudentlab.doc)* students read a scenario in which a patient receives news about the results from a

genetic test for brain cancer and receives input from a genetic counselor regarding the significance of those results. Students discuss the role of genetic counseling and patient information as a group and produce an outline of the ethical considerations that a genetic counselor should keep in mind, basing their findings on what they now know can go wrong in a multi-step lab procedure. This in turn will help them evaluate the validity of genetic test results based on the complications that could arise from the testing procedures. Students research the tests employed during the genetic screen for cancer, how these tests work, and the strengths and weaknesses for each. Individually, students will utilize the knowledge gained their own DNA analysis of human hair to evaluate genetic tests available for cancers. They will produce a folder in which each of several test methods are outlined as well as strengths, weaknesses, common uses, and cost.
*****instructor guide available for case after obtaining a free login account at Bio-link.org

### 3: Statistical Analysis of Population Data Activity

In the previous assignment, students discussed the statistical relevance of data (It's as Easy as Pulling Hair), in this assignment the students will perform their own statistical analysis of M&Ms. Students will study statistical frequency and relevance through an activity such as "Quality Control in the M&M Factory" (http://www.bio-link.org/home2/search/content/M%26M%20factory). Students analyze M&Ms for statistical frequency of color and quality and calculate ratios and produce valid histograms of their data from the experiment. With this better understanding of statistically significant data, students return to the "It's as Easy as Pulling Hair" activity to develop a "Genetic Counselor's Guide to Genetic Testing and Basic Statistics." Students will be divided into groups to work on units for this Guide Book, such as Pedigrees, Data Frequency, Histograms, DNA Tests, RNA Tests and so on.

## Unit 7: Evolution from Genetic perspective (Medical Biotechnology)

The theory of evolution is a foundational concept for biology, yet many students fail to grasp the true nature of this phenomenon. In this unit, students will explore the changes that take place in the DNA that drives phenotypic changes in individuals and, ultimately in populations. Students will use bacteria, with their quick generation time, to track the effect of a point mutation and to place "organisms" into related groups based on shared and diverging characteristics. These models will teach students relevant concepts and vocabulary. As students progress through the unit, they learn about the polymerase chain reaction and search genetic databases to find similarities in DNA sequences which can determine a specific identification or relation to the submitted sequence. Finally, students investigate the human population and the implications for changes in DNA that may be beneficial in some instances but harmful in others.

## Unit 7: Key Assignments

### 1: Point Mutation Leading to Streptomycin Resistance in E. coli (Lab)

In this activity, students perform a laboratory investigation that demonstrates a spontaneous point mutation for streptomycin resistance in a culture of *E. coli* bacteria. The students pour streptomycin containing gradient plates, plate the bacteria, and examine the plates for growth. Students then test their plate colonies for resistance by growing in a medium containing streptomycin. Students use their knowledge of point mutations in the development of new alleles and the selection driving the evolution of population change to describe the shift of the laboratory *E. coli* population from one that was largely sensitive to the antibiotic to one that is now resistant. They will also research scientific publications to find examples of current antibiotic resistance. Using a multimedia presentation format, they present their laboratory findings and its connection to their investigative research.

### 2: DNA Barcode PCR Lab

After learning about phylogeny, cladistics, and classifications, students now learn to identify a plant based on its DNA and to determine its evolutionary relationship to other plants based on genetic sequences. Using their knowledge of DNA structure, mutations, and phylogenetic relationships gained from the earlier work, students will amplify a segment of a gene, learn about DNA databases, identify an unknown plant sample and investigate genetic relationships. Students first collect plant samples from a designated area, extract DNA, then amplify a segment of the *rbcL* gene using polymerase chain reaction (PCR) to create unique barcodes. These amplified sequences are then submitted for sequencing and the resulting sequences are submitted for sequence alignment and species identification using online tools such as DNA Subway. Students will work in groups to generate a cladogram of their plant species based on their obtained DNA sequences.

### 3: Are Gene Mutations Good or Bad for the Population

In this assignment, students examine sickle cell disease from a genetic perspective. Students will begin by watching the HHMI video on sickle cell disease (http://www.hhmi.org/biointeractive/sickle-cell-anemia). This video demonstrates the link between a genetic mutation and the resulting change in hemoglobin and red blood cell structure. Following this students will explore the connection between gene alleles and genetic selection using sickle cell disease as an example. An example of a reading selection for this topic for this is "Survival of the Sickest" (https://www.amazon.com/Survival-Sickest-Surprising-Connections-Longevity/dp/0060889667) or "Just a Theory" AIDS vs CCR5 receptor (https://www.amazon.com/Just-Theory-Exploring-Nature-Science-ebook/dp/B009L28

SX4/ref=mt_kindle?_encoding=UTF8&me=). An additional option would be for students to watch the HHMI video, *The Making of the Fittest: Natural Selection in Humans* (http://www.hhmi.org/biointeractive/making-fittest-natural-selection-human). Following these activities, students will prepare an opinion paper about whether mutation is good or bad for the human population and prepare for a panel discussion. (Option: An outside expert could act as a facilitator of the discussion.)

**Unit 8: Basic Physiology (Animal Biotechnology/ Medical/ Nanobiotechnology)**

In this unit, students will use biotechnological approaches to study and diagnose human illnesses and disease. The medical application of biotech techniques has created entire industries based on diagnosis and screening, everywhere from hospitals to companies offering direct to consumer genetic testing. An ELISA assay, a common procedure in diagnosing illness and disease, will be conducted during a wet lab simulating patient screening for HIV. Students will follow-up by examining the ethical questions surrounding the information it provides and discuss their perspectives in a socratic seminar. In the process students will examine the structure and function of the human immune system and the application of immunotechnology to *in vitro* techniques.

**Unit 8: Key Assignments**

**1: Pathogen Screening - ELISA technique Lab**

ELISA is a widely used antibody-based laboratory assay technique used to screen samples and patients for various illnesses and infectious diseases. In this lab, students will conduct an ELISA assay using a commercially available kit (Bio Rad - ELISA explorer) and screen various samples for the presence of a simulated pathogen, such as HIV. Students will conduct, gather, and interpret electrophoresis data to identify positive and negative samples. As an alternative to a lab report, students complete a medical report for a fictional patient and provide their assessment and conclusions about the information provided by the test. By replacing a standard lab report with the more authentic medical report, students gain valuable context and perspective for the ethical questions to follow.

**2: Ethics - Who has a right to know/to test?**

Tying in to the results of the previous assignment, students will examine the question of who has a right to know the results, or order the taking of medical screening tests. As part of a socratic seminar, students discuss the pros and cons of various case studies dealing with scenarios including disclosure of screening results to family members, employers, and the public. In order to expand the discussion and address a range of topics, different cases should be assigned to groups of students to be discussed while others observe. Other perspectives could include the legal and ethical responsibilities of

physicians in disclosing test results as well as the issue of whether testing can, or should, be mandatory for various civil rights, such as employment. This is an opportunity for students to effectively use evidence in the service of making arguments in their discussion. Students conclude by demonstrating use of supporting evidence and examples in a written summary.

## Unit 9: Introduction to Energy/Metabolism

In this unit, students will explore the complex enzymatic systems that result in two key metabolic processes: cellular respiration and photosynthesis. Through laboratory activities, they will visualize the effects of these processes under different conditions. In addition, they explore the implications of genetically modifying organisms in order to precisely change a gene, a process that alters the metabolism of that organism and that carries numerous ethical concerns/implications. Finally, they will debate what regulations should be in place in the United States to govern the development and marketing of GMOs.

## Unit 9: Key Assignments

### 1: Cellular Respiration and Photosynthesis:

Students perform investigations that identify similarities and differences between the structures of a chloroplast and mitochondrion and the relationship between photosynthesis and cellular respiration in order to understand key metabolic processes. Students will use colorimetric pH indicators to track alkalization or acidification of a solution due to $CO_2$ consumed during photosynthesis or $CO_2$ produced during cellular respiration. Algal beads or any other photosynthetic organism will be used with the colorimetric pH indicator solution to explore how the opposing and interconnected photosynthesis and cellular respiration processes work together in a single organism. Students will investigate how various factors such as light color, light intensity, temperature can affect one or both of these processes. Students will go through the scientific inquiry process such as asking questions, posing hypotheses, designing experiments, analyzing data and communicating findings. They will predict their outcomes and then perform the experiments. After all the data has been collected, students will present their data in a table which clearly shows the relationship between variables and data points. Students make conceptual connections between photosynthesis and cellular respiration incorporating generated data and some provided evidence to write a discussion section for a research paper in which they must demonstrate how their data supports that photosynthesis and cellular respiration are related to desired traits of animals or crop plants.

**2: Ethics**:
Organisms can undergo genetic modification for the purpose of improving traits or correcting inborn errors of metabolism (eg., for plants-more biomass under stressful conditions or more nutrients, or for animals and humans correcting a genetic flaw that causes a metabolic disorder). Genetically Modified Organisms (GMOs) and gene therapy are technological advances that have been made possible due to the tools of genetic engineering. After completing work in previous units and assignment 1, students now understand the link between DNA, genes, enzymes, and metabolic processes. In this assignment, students will explore the ethical arguments in favor and against the use of genetic modification of organisms. In the European Union, the sentiment is different from that of the United States regarding GMOs and students will explore the political and marketing events that have generated this phenomenon by visiting reliable websites such as http://www.umass.edu/sts/ethics/online/cases/GMO/case.html. Students will investigate the types of genetically modified organisms that have been marketed or gene therapies that have been utilized, as well as the development of organisms and therapies that have yet to be used for their intended purposes while paying special attention to the effects on metabolism. Students can determine what government regulations and market forces are at play that may prevent a promising organism or therapy from being utilized. Ultimately, students will form teams and debate what regulations should be in place in the United States concerning the development and marketing of GMOs and gene therapy.

**Unit 10: Culminating Final Project**
The manufacture of biologic therapies is a highly demanding process that is becoming increasingly important in our society. The capstone experience will employ a variety of laboratory procedures in an integrated project to produce a protein product while emphasizing the use of SOPs, cGLP, laboratory documentation and laboratory safety. This project mirrors, on a small scale, the entire industrial process of producing a biopharmaceutical product (therapeutic protein) to treat a variety of diseases. The capstone may be accomplished by using the Amgen Biotech Experience (ABE) curriculum or another project of similar design. The capstone project intends for students to gain a clear understanding of how to use recombinant DNA techniques to introduce new genes into an organism and have that organism produce new proteins. The model system uses a gene from a sea anemone that encodes a red fluorescent protein which is spliced into an expression vector, the vector is then introduced into an *E. coli* strain thereby producing a genetically engineered organism. The encoded protein is then produced by the bacteria and purified. This project models how the process can be used with a human gene to produce proteins to treat a human disorder

such as insulin to treat diabetes or human growth hormone to treat stunted growth conditions. The final result of the project is a report in the form of a scientific publication.

## Unit 10: Key Assignments

### 1: Restriction enzymes, ligases, and vectors.

Students carry out a laboratory activity where they use key enzymatic tools of genetic engineering to create a recombinant plasmid and document all hypotheses, procedures and results in their lab notebook. First, students use restriction enzymes such as BamHI and HindIII to digest two plasmids. Students predict the DNA fragments that will result from the lab protocol and then verify the result with gel electrophoresis using DNA ladders. The gel should be photographed and the image printed for inclusion in their laboratory notebook and the final assignment. Next, the students use DNA ligase, with the goal of joining DNA fragments to the correct position in the expression vector with the goal of producing a functional plasmid that contains the gene of interest and a gene providing resistance to an antibiotic such as ampicillin. Students predict the various plasmid configurations that may result from ligation and verify the possibilities by comparing results seen after gel electrophoresis. Once again, the image will be used as documentation in the laboratory notebook. Students use documented procedures, hypotheses and findings (including photographs) to construct both a materials and a results section for the final assignment.

### 2: Transformation and Production of Product

Students will use their newly engineered plasmid to produce a protein product. Laboratory procedures will include the introduction of the newly engineered plasmid into bacterial cells utilizing a standard industry method for cell transformation. Bacterial cells with the plasmid will be selected for using the antibiotic resistance engineered into the plasmid. Students will utilize this genetically modified organism to express their protein of interest. Student groups will record their transformation and bacterial growth conditions in their laboratory notebooks. Variables such as temperature, time, concentration of inducer, and cell density will be recorded, analyzed, and added to their methods and their results section of their final report.

### 3: Purification of Product

Following protein expression by the students in their bacterial expression system, the students purify and quantitate their protein of interest. Utilizing column chromatography, students will investigate how their protein of interest can be separated from the other proteins in the cells by this purification process. Samples from the chromatography column will be collected in aliquots to be used to quantify the yield of their purified protein. Native-PAGE and SDS-PAGE could be used to visualize the

protein contained in the aliquots. The gel will be photographed and documented in the student's lab notebook. Following this, students also collect data on protein concentration using the spectrophotometer. The students will analyze this photograph to determine the yield and purity of their protein and compare this information with the data they collected from the spectrophotometer. Their final report will contain a section on the comparison of these results. To help students think about the value of the "product" they have manufactured and purified the students record the total amount of protein produced, protein concentration, protein purity, lab hours spent in the process and materials used to make their product. Then students research the price of the protein if they were to buy it from a vendor and calculate how much profit they would have made if they were to sell their product. After they write a summary of their findings that may serve as a portion of the introduction in their final assignment.

### 4: Challenges in Biological Therapeutic Manufacture

Students will engage in literature and informational website research to investigate challenges in biological therapeutic manufacture. Challenges include production problems and recalls, safety concerns arising during development but after significant investment of funds, and funding issues for projects such as orphan drugs. Students produce a report in the form of a graphic organizer in which they identify instances of industrial challenges, the cause of those challenges and the outcomes of the incidence. Students should examine the ethical considerations regarding the course of action to take with attention to potential harm to patients, protecting financial investments, and providing potential relief from devastating diseases with small affected populations.This report will be shared with the class and used to help form a discussion section in the final assignment.

### Final Assignment: Journal Article

Scientific publications in the form of peer reviewed journal articles are key to the advancement and distribution of scientific knowledge. Students will use the information they have compiled in their laboratory notebook and in their outside investigations from assignment 5 to produce a report on the capstone project that takes the form of a scientific journal article. The article will include an abstract, introduction, materials and methods, results, discussion that includes their conclusion and a reference section. The information contained within the report should include citations. This report will require research to find relevant scientific publications that relate to the introduction, methods, and discussion section of the report. As an optional culminating experience, students could present their papers during a mock scientific conference to their peers while relating their project to different areas of biotechnology (eg., human therapeutic production or research and development).

**Course Materials:**

Introduction to Biotechnology (3rd Edition) by William J. Thieman and Michael A. Palladino (Jan 23, 2012) ISBN 978-0321766113

Campbell Essential Biology (5th Edition) by Eric J. Simon, Jean L. Dickey and Jane B. Reece (Feb 19, 2012) ISBN 978-0321772596

Campbell Essential Biology with Physiology, Simon, Eric J., Reese, Jane B. and Dickey, Jean L. Campbell Essential Biology with Physiology, 3rd ed. Benjamin Cummings, 2010, ISBN: 0321602072

Biology by Sylvia Mader and Michael Windelspecht (Jan 3, 2012) Natu

Nature Publishing Group's "Priniciples of Biology" (online text with lifetime access): www.nature.com/principles