TEACHING THE GENOME GENERATION™

CURRICULUM OVERVIEW

This document will introduce you to Teaching the Genome Generation™ (TtGG) and help you determine which components best fit your curriculum needs. If you have any questions or wish to implement TtGG, contact *ttgg@jax.org*.

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PROGRAM OVERVIEW AND LEARNING GOALS

Teaching the Genome Generation (TtGG) was designed to provide high school teachers the content knowledge, teaching strategies, and resources needed to enhance student learning in genomics and personalized medicine. This program will provide instruction in molecular genetics, the use of bioinformatic tools, and the discussion of the ethics of genetics research. Teachers will develop lessons designed for their unique school environment and resources. Through the TtGG community, teachers will have access to additional resources and expert assistance during the academic year.

The program is divided into three major branches, which should be taught in an integrated fashion, not as isolated units. These topics are: 1) the ethics involved in DNA testing (both in the classroom and the community), 2) the methods involved in isolating, amplifying, and detecting DNA, and 3) the bioinformatic methods utilized in analyzing DNA, RNA, and amino acid sequences. Bioethics lessons and resources are provided in collaboration with the Personal Genetics Education Project (pgEd) at Harvard Medical School. Additionally, TtGG lab exercises utilize human genes, rather than genes from bacteria or other animals, which connects students to the material presented and allows them to take ownership of the results.

By engaging in laboratory, bioethics, and bioinformatics professional development, participating teachers will increase their ability to teach complex concepts of genomics and bioethics to students. Consequently, students exposed to the TtGG content will demonstrate an enhanced understanding of genomics content and will be more likely to have positive attitudes towards and participate in future STEM courses.

An online version of the TtGG program is available at no cost to current teachers, as well as teachers new to TtGG. Experience the full curriculum, plus knowledge check quizzes and planning assignments. Visit *www.jax.org/TtGG* for more information.

The Jackson Laboratory Genomic Education division specializes in developing lessons, activities, and hands-on laboratory protocols for teaching and learning about genetics and genomics. Find the TtGG lessons and more on our website: *www.jax.org/stem-resources*

LEARNING GOALS

After completing the TtGG program, teachers will be able to:

1. Perform modern laboratory techniques and properly use laboratory equipment.
2. Interpret DNA gels and sequence data to infer genotypes for several common human variants.
3. Navigate common bioinformatics databases, which are rich sources of information for new lessons.
4. Teach the ethical concerns surrounding personalized medicine, including informed consent.

Student learning goals are identified at the beginning of each protocol.

Program Acknowledgments

This program was designed and is maintained by the TtGG Team at The Jackson Laboratory, including Charlie Wray, Ph.D.; Sarah Wojiski, Ph.D.; Erica Gerace, Ph.D.; Emaly Piecuch, Ph.D.; Christina Vallianatos, Ph.D.; and Alexa Wnorowski, Ph.D. These protocols were modified for classroom use by Barbara Farrell, formerly of North Yarmouth Academy. TtGG is supported by the NIH/National Institute of General Medical Sciences Science Education Partnership Award (SEPA), the Petit Family Foundation, and an anonymous gift.

INTRODUCTION TO PERSONALIZED MEDICINE

Medicine as we know it is undergoing a revolution due to the promise of the emerging field of genomics. Through analysis of large DNA sequence databases, scientists are realizing the extent of genetic variation among humans and how those variants can affect an individual's health and their response to treatment. Medicine is no longer one size fits all; it's personal. Patients and their doctors can elect to submit samples for genetic tests (which would return results based on a single gene) or genomic tests (in which a panel of genes or a whole genome can be sequenced). These results can help guide patient lifestyle for disease prevention or direct treatment of disease. One such gene of medical importance is CYP2C19, a gene involved in drug metabolism, which is available for study through TtGG. Variants in this gene can cause slow metabolism or decreased activation of therapeutic drugs. With access to this kind of information, patients and their doctors are empowered to make informed decisions concerning treatment. This could save both valuable time in disease recovery and money, not only in the medical industry, but also from the patient's pocket.

Through TtGG, teachers and students will explore ethical considerations associated with personalized medicine by engaging in classroom discussion (supplemented by pgEd lesson plans) about the handling of their personal samples.

ETHICAL CONSIDERATIONS

The use of humans or human samples in research has always been a point of debate and concern. Scientists have learned about the ethical implications of research on human samples throughout the long history of biological research. Today, there are many regulations that researchers must follow, including protecting the privacy of the human subject. DNA sequence (genotype) falls into that category since it inherently carries the information that describes who an individual is. Therefore, the unique genetic signature of an individual must be protected from broad dissemination and misuse. Individuals can elect to have their genetic information distributed throughout the research community, but they must provide informed consent, typically by signing a written document that confirms they understand all intended future use of the human sample.

The TtGG DNA EXTRACTION PROTOCOL uses saliva, and the cheek cells therein, as a source for extracting purified human DNA. In order to maintain anonymity and protect the personal information of students providing a DNA sample, the donation must be **voluntary** and collected in a manner that maintains anonymity.

BIOINFORMATICS AND DATA ANALYSIS

Bioinformatics is an organized and accessible mechanism of dealing with biological data and information, blending molecular biology with computer science. Modern genomics research generates vast amounts of DNA sequence data. Bioinformatics (and bioinformaticians!) are needed to manage this data and help propel scientific discoveries.

TtGG exercises serve to introduce students to this exciting field and career path. Choosing to study ACTN3, CYP2C19, or TAS2R38 in the TtGG labs will lead classes to the SEQUENCE ANALYSIS PROTOCOL. Students will download and explore Sanger DNA sequencing files to examine genomes nucleotide by nucleotide.

TtGG also offers four classroom-based (non-laboratory) modules in bioinformatics and genomics emphasizing data and math literacy. These modules introduce students to navigating genomics databases, using bioinformatics tools, and performing biologically-relevant calculations through the lens of cancer genomics, sequence identity, new variation in the genome, and genetic ancestry.

Additionally, the Case Study of Dr. James Lupski is based upon the true story and takes student on a hunt for the genetic cause of a medical mystery. Other bioinformatics and data analysis activities include searching databases, sequence identification, and interspecies comparison of DNA and amino acid sequences. These exercises are suitable for interactive in-class, asynchronous, and/or virtual classroom settings.

INTEGRATING TtGG INTO YOUR CLASSROOM

The information presented in TtGG is critical for developing a scientifically literate population in the emerging genomics era. There are many ways in which this material can be disseminated to students, including both science and non-science classes. The TtGG team is happy to help you modify the curriculum to fit your needs.

Examples could include:

1. Stand-alone Genomics course
2. Parts of the protocols in advanced classes, such as AP Biology
3. Basic genetics/genomics content in introductory biology classes
4. Bioinformatics and data analysis activities in advanced classes or in Statistics or Mathematics courses
5. Ethics component in cross curricular classes:
    - Health class — personalized medicine
    - History — eugenics
    - Civics — politics, law, economics, voter information
    - DNA Forensics

Lesson Plan	NGSS Alignment
Bioethics Lessons (pgEd)	Aligned to NGSS and Common Core within each lesson
DNA Extraction Laboratory Protocol	HS-LS1-1, HS-LS1.A, HS-LS3-1, HS-LS3-2
PCR Laboratory Protocol	HS-LS1-1, HS-LS1.A, HS-LS3-1, HS-LS3.A, HS-LS3-2
Restriction Digestion Laboratory Protocol	HS-LS1-1, HS-LS3-1, HS-LS3-2
Gel Electrophoresis Laboratory Protocol	HS-LS1-1, HS-LS3-1, HS-LS3-2, HS-LS3-3, HS-LS3.B
Sequence Analysis Laboratory Protocol	HS-LS1-1, HS-LS3-3, HS-LS3.A, HS-LS3.B, HS-LS4-1
Bioinformatics and Data Analysis Lessons	Aligned to NGSS within each module

EXTENSIONS TO LEARNING WITH TtGG

While this curriculum will satisfy the learning needs of many classrooms, perhaps you would like to make a curricular link to other subjects, or maybe an introduction to genetic analysis will inspire some of your students to dig deeper. We recognize the need for continual innovation in our offerings. Therefore, we welcome the opportunity to aid you in the development of lesson plans for content and skills extension. Of course, lesson plans take time, so please contact us at *ttgg@jax.org* four weeks ahead of your intended date of implementation.

If you buy your own molecular equipment, extensions to the learning are endless! Several of our teachers have been able to purchase some or all of our suggested equipment through school budgets or grant opportunities. You can utilize DNA amplification, gel electrophoresis, restriction digestion, and sequencing to perform experiments in microbiology, antibiotic resistance, genetic engineering, population genetics, evolution, forensics, and plant genetics, to name a few!

Finally, some advanced students may want to perform independent projects for a local science fair or competition, a graduation requirement, or personal inquiry. Contact us at *ttgg@jax.org* to find out if we can support your budding scientists with projects related to the TtGG curriculum.

INVALUABLE LABORATORY EXPERIENCE

The process of experimentation and performance of laboratory skills is vital for all students, whether they continue in the sciences or simply act as advocates for their own health. Knowledge and understanding of scientific practices grounds the discipline in reality rather than seeming like magic (as seen on many television programs). The following protocols were designed as a series of experiments so students can follow the process from DNA collection to DNA sequencing. Teachers can choose from five genes to investigate in the lab. Each of these genes and their variants were selected due to their interesting phenotypes, their lack of connection to human genetic disease, and their different variant structures. Select one or a few genes to study with your students!

Target gene options

ACE Insertion/deletion of Alu sequence repeat within an intron

Associated with endurance in long distance events

ACTN3 Single nucleotide polymorphism (SNP) within an exon, one variant produces shortened protein

Associated with athletic performance

CYP2C19 SNP within an exon, one variant introduces a splice site resulting in frameshift

Affects ability to metabolize certain drugs into active form

OXTR SNP within an intron, no effect on protein coding sequence

Associated with social behaviors

TAS2R38 Three SNPs in protein coding sequence

Affects ability to taste certain bitter compounds

REQUIRED CLASSROOM MATERIALS

- Ice bath or crushed ice
- Refrigerator
- Freezer

PROVIDED BY JAX

For these materials, please contact ttgg@jax.org

- Teacher and Student versions of each laboratory protocol
- Gene information sheets
- All equipment, reagents, and consumables necessary
- Technical and content support

TEACHER VERSIONS OF PROTOCOLS

These protocols provide additional information regarding the theory behind the process, sample storage recommendations, tips and tricks, examples of results, troubleshooting, and time requirements. Additionally, Curriculum Integration and Planning Notes sections in each protocol allow teachers to reflect on how TtGG exercises can be used in each unique class they teach.

STUDENT VERSIONS OF PROTOCOLS

These protocols exclude answers and the supplementary information provided in the Teacher version. Additionally, students have free space to document alterations to the procedures.

DNA EXTRACTION PROTOCOL (all genes)

Genetics analysis starts with DNA isolation. Students have the opportunity to collect human samples (saliva and cheek cells) as a source for extracting human DNA. The "long" version of the protcol results in a purified DNA product. The "quick" version provides a shorter option as a 20 minute heat-based DNA isolation. User beware: the quick method produces less pure DNA than the long method, so the DNA will degrade overnight.

In order to maintain anonymity and protect the personal information of students providing a DNA sample, the sample donation must be voluntary regardless of protocol used.

Skills learned: DNA collection and extraction, micropipetting, and centrifugation.

Protocol Structure

STEP 1	8 minute video
	Break point if needed
STEPS 2-8	20 minutes
	Break point if needed
STEP 9	90 minute incubation
	Break point if needed
STEPS 10-30	60-70 minutes
	Break point if needed
STEPS 31-32	5 minutes

PCR PROTOCOL (all genes)

DNA samples isolated in the DNA EXTRACTION PROTOCOL contain genomic DNA from each anonymous donor. Each sample undergoes polymerase chain reaction (PCR) to both target and amplify the TtGG gene region of interest. This creates enough copies of variant DNA segment to run downstream lab procols, including restriction digest, gel electrophoresis and/or DNA sequencing.

Skills learned: micropipetting, PCR master mix preparation, use of thermal cycler, and centrifugation.

Protocol Structure

STEPS 1-6	25 minutes
	Break point if needed
STEPS 7-12	25 minutes
	Break point if needed
STEPS 13-18	Several hour incubation
	Break point if needed

RESTRICTION DIGEST PROTOCOL (CYP2C19 or OXTR)

Variants examined in CYP2C19 and OXTR may create or ablate a restriction enzyme cut site, and can aid in genotyping samples. Amplified DNA samples undergo a restriction enzyme digest before then visualizing in the GEL ELECTROPHORESIS PROTOCOL to determine which variants are present.

Skills learned: micropipetting and restriction enzyme digestion.

Protocol Structure

STEPS 1-6	15 minutes
	Break point if needed
STEPS 7-12	2 minutes

GEL ELECTROPHORESIS PROTOCOL (all genes)

All amplified DNA samples from the PCR PROTOCOL and samples from the RESTRICTION DIGEST PROTOCOL are finally visualized using agarose gels. The presence of bands at the expected size(s) will indicate that the PCR was successful (all genes). Genotypes may be determined from the pattern of DNA bands observed (ACE, CYP2C19 and OXTR only). Some DNA samples will require DNA Sanger Sequencing and Analysis to determine what genotypes are present (ACTN3 and TAS2R38), but still must be checked by gel electrophoresis to ensure the PCR products are as expected.

Skills learned: micropipetting, agarose gel electrophoresis, and data interpretation.

Protocol Structure

ALL STEPS 30 minutes

SEQUENCE ANALYSIS (ACTN3, TAS2R38 or CYP2C19)

DNA sequence files provided by The Jackson Laboratory are used to find variants, create contiguous sequence constructs, and compared to known sequences in databases.

Skills learned: bioinformatics and data interpretation.

Protocol Structure

STEPS 1-14 15 minutes

Break point if needed

STEPS 15-17 35 minutes

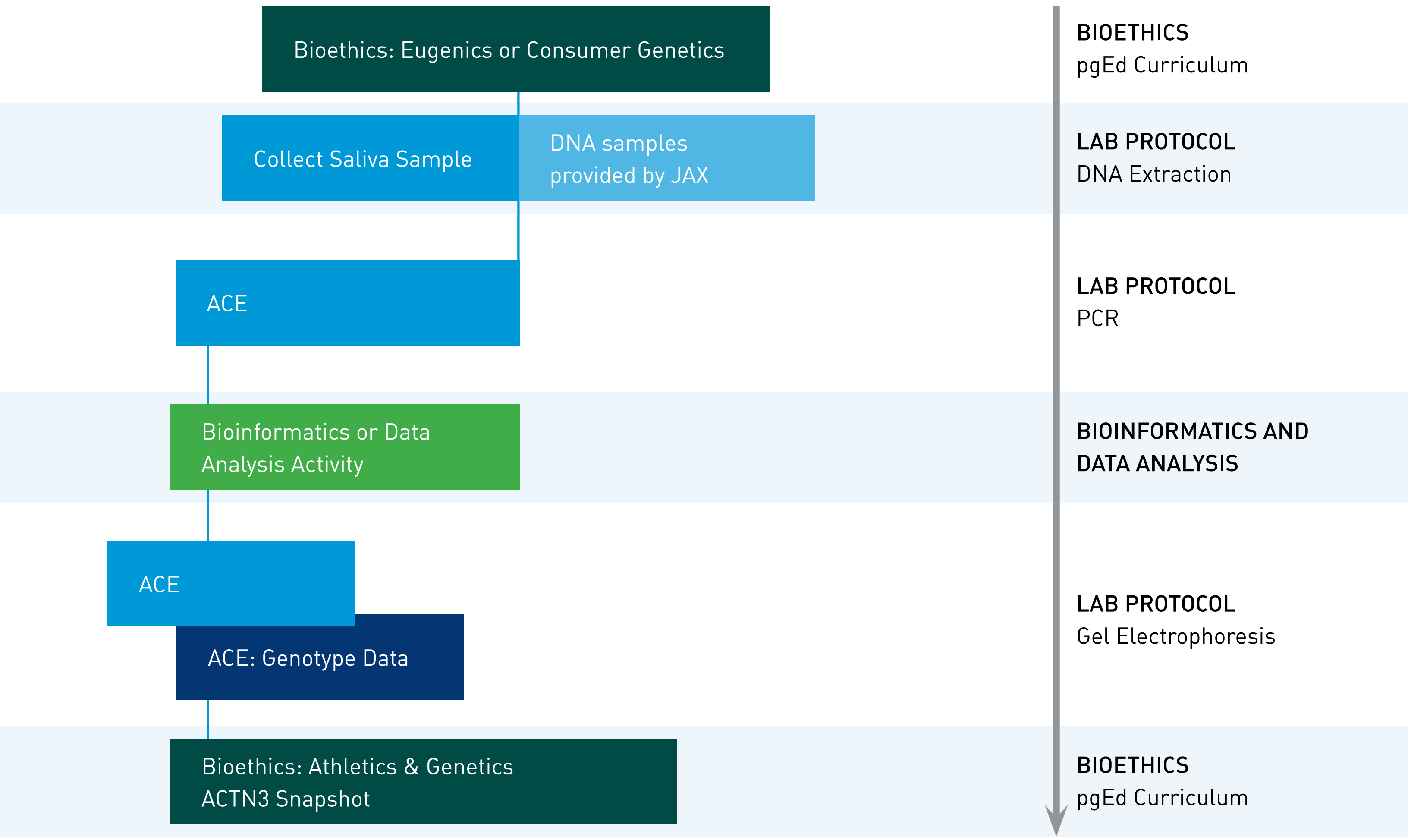
Break point if needed

STEPS 18-23 40 minutes

CURRICULUM PATHWAY 1

The quickest pathway from DNA samples to genotype data focuses on the ACE gene. Students can experience DNA extraction, amplification, and detection through gel electrophoresis.

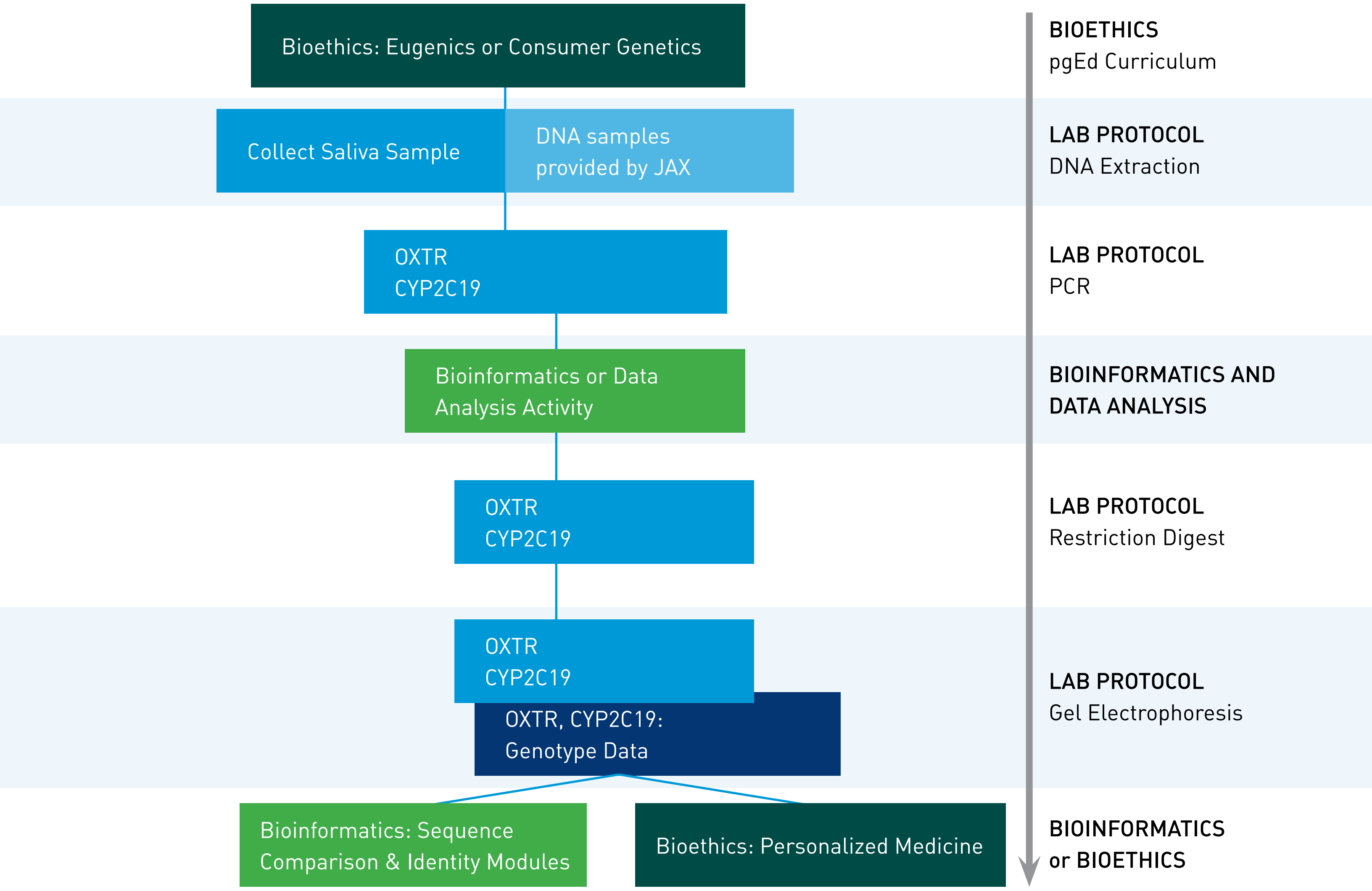
Suggested Student Level: Introductory Biology



CURRICULUM PATHWAY 2

In this intermediate pathway, you have a choice in the focus gene. Regardless of gene, students can experience DNA extraction, amplification, restriction digestion, and detection through gel electrophoresis.

Suggested Student Level: Honors or AP Biology



CURRICULUM PATHWAY 3

This advanced pathway once again allows for choice in the gene of interest. In addition to the intermediate techniques, students will practice bioinformatics analysis on DNA sequences from the selected gene.

Suggested Student Level: Elective Biology