

## 1

# What is Genetic Research?

## Introduction

In this lesson, students are introduced to the process of genetic research. The lesson begins with a Think-Pair-Share activity designed to introduce students to the types of research questions people in different career fields might answer using **bioinformatics** tools. After a short background explanation provided by the teacher about how genetic research is done, students make their own **hypotheses** and predictions about the relatedness of canine species, and align paper DNA sequences to evaluate their hypotheses. The lesson concludes with a group activity introducing students to **pairwise comparisons** of DNA sequences, which will be explored more fully in later lessons. In *Lesson One*, students also learn how **DNA sequencing core lab managers** might use bioinformatics tools in their career.

## Learning Objectives

At the end of this lesson, students will know that:

- Bioinformatics tools are used by people in many different career fields, including DNA sequencing core lab managers.
- The key components of the scientific research process are as follows: make observations about the natural world, develop a hypothesis, gather and analyze data, make conclusions, and revise your original hypothesis if needed.
- Technology advancements make it possible to collect large amounts of data; **data-driven research** is increasingly informing biological research.

At the end of this lesson, students will be able to:

- Develop research questions that can be answered with the tools of bioinformatics.
- Compare short DNA sequences to one another to identify nucleotide changes.
- Develop a conceptual map that charts out the basic steps involved in many kinds of genetic research, from DNA purification to DNA sequencing and analysis.

## Key Concepts

- Scientists in many different fields use bioinformatics to answer research questions specific to their field of study.
- Like many other kinds of research, genetic research is a **process**.
- Scientific experiments build on what is **already known** about a given subject or field, using this information and observations as background when asking scientific questions.

### Class Time

Two class periods of 50 minutes each, 100 minutes total.

### Prior Knowledge Needed

- DNA contains the genetic information that encodes traits.
- Basic knowledge of taxonomy (especially **genus** and **species**), and that the taxonomic hierarchy is derived from evolutionary relationships.
- Exposure to the Bio-ITEST Introductory curriculum, *Using Bioinformatics: Genetic Testing*, is highly recommended.

- The methods or practices of science (sometimes called the **scientific method**) involve: asking a question; developing a hypothesis about that question; gathering data; analyzing that data to determine whether the data support the hypothesis; making conclusions; and revising the original hypothesis if needed.
- Science today increasingly involves “data-driven” experiments, in which patterns or correlations are observed in large data sets, which inform hypothesis development and prediction.
- Scientific experiments build on one another, with both “successes” and “failures” helping to move the scientific process forward.
- Genetic research involves asking a research question based on observations of the natural world, including: analyses of large data sets; generating a hypothesis; predicting a result based on that hypothesis; obtaining or analyzing DNA sequence data; and comparing and analyzing DNA sequences to determine whether the prediction, and the hypothesis it was based on, were correct.

## Materials

Materials	Quantity
Teacher Resource— <i>Pairwise Comparisons of Canine DNA Sequences</i> , printed on a transparency <i>Optional: Provide as a Student Handout. See Procedures section Part II</i>	1 or 1 per student
Copies of Student Handout— <i>Bioinformatics: A Tool for Every Trade</i>	1 per student
Copies of Student Handout— <i>Careers in the Spotlight</i>	1 per student
Copies of Student Handout— <i>An Introduction to Genetic Research</i>	1 per student
Copies of Student Handout— <i>Canine DNA Sequences</i>	1 per student pair
Copies of Teacher Resource— <i>Canine DNA Sequences Species-Specific Masters</i> <i>Optional: See Teacher Preparation section</i>	1 set per 8 students
Copies of Student Handout— <i>The Process of Genetic Research</i>	1 per student
Teacher Answer Key— <i>Bioinformatics: A Tool for Every Trade</i>	1
Teacher Answer Key— <i>An Introduction to Genetic Research</i>	1
Teacher Answer Key— <i>The Process of Genetic Research</i>	1
Teacher Answer Key— <i>Pairwise Comparisons of Canine DNA Sequences</i>	1
Whiteboard or chalkboard and writing implements	1
Dry erase marker for use with Teacher Resource— <i>Pairwise Comparisons of Canine DNA Sequences</i> transparency	1
Pens or pencils	1 per student
Scissors	1 per student pair or small group
<i>Optional: Tape or glue sticks</i>	1 per student pair or small group
Overhead projector to display transparency Teacher Resource— <i>Pairwise Comparisons of Canine DNA Sequences</i>	1

### Computer Equipment, Files, Software, and Media

Computer and projector to display PowerPoint slides.

**Alternative:** Print PowerPoint slides onto transparencies and display with overhead projector.

*Lesson One* PowerPoint Slides—*The Process of Genetic Research*.

Available for download at: <http://www.nwabr.org/curriculum/advanced-bioinformatics-genetic-research>.

A student version of lesson materials (minus Teacher Answer Keys) is available from NWABR's Student Resource Center at: <http://www.nwabr.org/students/student-resource-center/instructional-materials/advanced-bioinformatics-genetic-research>.

**Optional:** "Sanger Method of DNA Sequencing" video freely available from the Howard Hughes Medical Institute (HHMI). Video is 51 seconds long and requires internet access and speakers to hear sound.

Available at: [http://www.hhmi.org/biointeractive/dna/DNAi\\_sanger\\_sequencing.html](http://www.hhmi.org/biointeractive/dna/DNAi_sanger_sequencing.html).

Computer lab with internet access and a word processing program such as Microsoft® Notepad or Word for answering homework questions.

## Teacher Preparation

- Load the classroom computer with the *Lesson One* PowerPoint slides and the "Sanger Method of DNA Sequencing" video (*optional*).
- Make one copy per student of each of the following *Student Handouts*: Student Handout—*Bioinformatics: A Tool for Every Trade*, Student Handout—*Careers in the Spotlight*, and Student Handout—*An Introduction to Genetic Research*.
- Make copies of Student Handout—*Canine DNA Sequences* for pairs or groups of students. Alternatively, make copies of Student Handout—*Canine DNA Sequences* or Teacher Resource—*Canine DNA Sequences Species-Specific Masters* (available at <http://www.nwabr.org/curriculum/advanced-bioinformatics-genetic-research>) and cut up DNA sequences in advance of class. Each species' DNA sequences can be kept in separate envelopes and distributed to students during class. Sequences may be laminated to increase their durability.
- *Optional:* Print Teacher Resource—*Pairwise Comparisons of Canine DNA Sequences* onto a transparency for use in *Part II* of the lesson. Alternatively, this table could be drawn on the board or projected with a document camera.

## Procedure

### PART I: Genetic Research, Research Questions, and Bioinformatics

1. Explain to students the **aims of this lesson**. Some teachers may find it useful to write the aims on the board.
  - a. **Lesson Aim:** Introduce students to the field of genetic research.
  - b. **Lesson Aim:** Review the practices of science.
  - c. **Lesson Aim:** Understand how **bioinformatics** is used in genetic research.

Teachers may also wish to discuss the *Learning Objectives* of the lesson, which are listed at the beginning of this lesson plan.

**Bioinformatics:** Bioinformatics is the application of computer science and information technology to biology and medicine. Bioinformatics combines computer science, mathematics, and biology to create methods for capturing, storing, analyzing, visualizing, and sharing biological data. Bioinformatics makes it possible to analyze large and complex biological data and can be used to search biological databases, compare sequences, and draw molecular structures.

2. Show the PowerPoint for *Lesson One*, beginning with **Slide #1**, “Genetic Research Deals with Inherited Traits.”

Genetic Research: **Slide #1**

### Genetic Research Deals with Inherited Traits

Genetic researchers study inherited traits by analyzing DNA sequences.

How are we similar?  
How are we different?

DNA isolation.

Use bioinformatics to research differences in DNA sequences.

Introduce students to the concepts of “genetic research” and “bioinformatics” by explaining the following:

- Genetic research deals specifically with inherited traits. These can be studied by analyzing DNA sequences (genetic data).
- Technological advancements have made it possible for scientists to collect large amounts of data much more quickly than ever before. For example, the Human Genome Project (completed in 2003) took over a decade to finish and cost \$2.7 billion dollars (about \$1 per DNA base). By building on DNA sequencing technology developed during the Human Genome Project, the newer next-generation DNA sequencing technologies make it possible to sequence thousands of DNA bases for the same cost. Sequencing a human genome can now be done in as little as a week and costs about \$1,000 – 2,000.
- Bioinformatics involves the tools and databases scientists use to store, analyze, and share biological data.
- Genetic researchers study **changes in DNA sequences**, which occur over time. For instance, when comparing the DNA sequence from the same gene among two or more species, the **number of changes in the DNA sequence is related to how long ago those two species diverged from one another**.
- Bioinformatics can be used by people in a number of different careers to answer a variety of research questions.

3. Show **Slide #2**, “Scientific Practices,” and review with students the steps involved in any scientific endeavor, as illustrated in the following example. If students are already familiar with scientific practices, teachers may wish to skip or shorten the following example.

**Scientific Practices**

**Ask a Question Based on Observations:**  
*Plants grow in soil. What do plants use to grow larger?*

**Hypothesis & Prediction:** If – and – then  
*Hypothesis: Plants use materials in the soil to gain mass.  
Prediction: **If** my hypothesis is correct, **and** I measure the mass of soil & plants over time, **then** I predict the soil mass will decrease as plant mass increases.*


**Gather and Analyze Data (Methods):**  
*Measure mass of bean seeds and soil at Day 1 and Day 15.*

**Results:**  
*Bean plants increased in mass by 24.6 grams. Soil mass stayed the same.*

**Conclusions:**  
*Minerals from the soil do not affect the mass of plants.  
Hypothesis is contradicted.*

**New Hypothesis:**  
*Plants use something in the air to gain mass.*

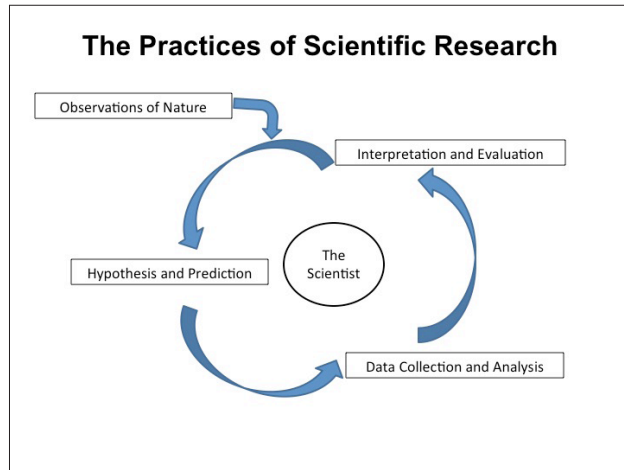
Image Source: Wikipedia Commons



- **Observations of nature** inform much of science. Scientists observe patterns or phenomena they seek to understand.  
*For example, we observe that plants grow in soil.*
  - Ask a **question** based on observations of the natural world.  
*What contributes most to the mass of the plant? Is it the soil?*
  - Develop a **hypothesis** about your question and observations. Often the “if-and-then” format is used. **If** your hypothesis is correct **and** you perform an experiment, **then** you should get a particular result (prediction).  
**Hypothesis:** *Plants use minerals in the soil to gain mass.*  
**Prediction:** *If my hypothesis is correct (plants use minerals in the soil to gain mass), and I measure the mass of seeds and soil before and after growth, then I predict that the mass of the soil will decrease as the plant mass increases because plants are absorbing minerals from the soil.*
  - **Gather and analyze your data** to see if it supports your hypothesis. These are described in your **Methods**.  
*Seeds were planted in pots and the mass of bean seeds and the soil at Day 1 and Day 15 were measured.*
  - Report your **Results**.  
*Bean plants increased in mass by an average of 24.6 grams. The mass of the soil stayed the same.*
  - Make **Conclusions** about your hypothesis based on your results.  
*Minerals from the soil do not affect the mass of plants. Hypothesis is contradicted or not supported by the data.*
  - Make a **new hypothesis** if needed.  
*Plants use something in the air to gain mass.*
4. Show **Slide #3**, which illustrates “The Practices of Scientific Research.” Emphasize to students that research is a **process**: it begins with a hypothesis and prediction (experiment), after which scientists gather and analyze data, and interpret or evaluate that data before making their next prediction.

**Hypothesis:** A proposed, testable, tentative explanation or relationship for certain facts about the natural world, based on observation.

Genetic Research: *Slide #3*



5. Show *Slide #4*, “What is Bioinformatics?” and review the definition of bioinformatics with students. Bioinformatics is the application of computer science and information technology to biology and medicine. Teachers may wish to explain this further by telling students that bioinformatics combines computer science, mathematics, and biology to create methods for capturing, storing, analyzing, visualizing, and sharing biological data.

Genetic Research: *Slide #4*

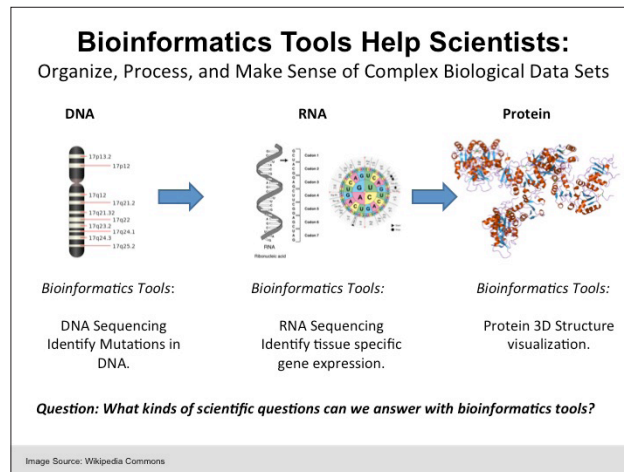
**What is Bioinformatics?**

Bioinformatics is the application of computer science and information technology to biology and medicine.

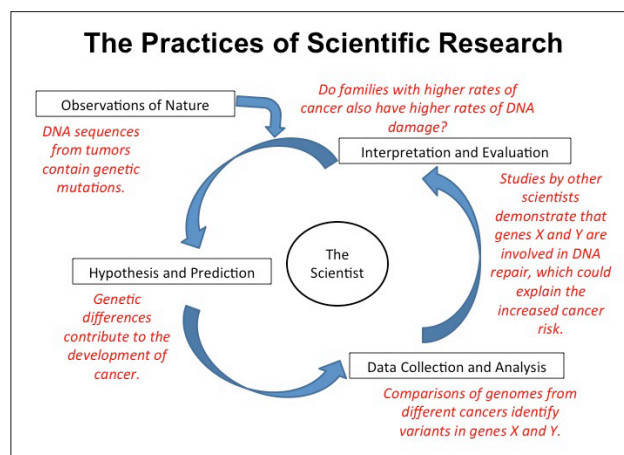
Bioinformatics makes it possible to analyze large quantities of complex biological data and can be used to **search biological databases, compare sequences, and draw molecular structures.**

6. Advance the animation by clicking the forward arrow on the computer projecting the PowerPoint slides. A second statement about the power of bioinformatics will appear: “Bioinformatics makes it possible to analyze large quantities of complex biological data and can be used to **search biological databases, compare sequences, and draw molecular structures.**”
7. Show students *Slide #5*, “Bioinformatics Tools Help Scientists Organize, Process, and Make Sense of Large Biological Data Sets,” which lists bioinformatics tools specific to different kinds of biological molecules. Tell students that they will be using many of the tools mentioned in this slide, such as tools to analyze DNA sequences and the Cn3D program to analyze protein structures.

Genetic Research: *Slide #5*



Genetic Research: *Slide #6*



8. Show *Slide #6*, “The Practices of Scientific Research,” which provides an example of the types of questions and scientific methods based on the observation: **DNA sequences from tumors contain genetic mutations.** Bioinformatics makes it possible to compare DNA sequences or whole genome sequences from individual tumors.

- This observation could lead to the **hypothesis** that these genetic differences lead to the development of cancer. **If** genetic differences contribute to cancer **and** we sequence the genomes of multiple tumors, **then** I predict that common genetic differences among tumors will be found.
- **Collecting and analyzing data**, in the form of genome sequences from multiple tumors, reveals genetic differences or variants in two key genes, X and Y.
- **Interpretation and evaluation:** Building on data from other scientists, who demonstrated that genes X and Y are involved in DNA repair, scientists conclude that the genetic differences in genes X and Y could have led to the development of cancer due to increased rates of DNA damage.
- This interpretation leads to the next **prediction**, that families with higher rates of cancer also have higher rates of DNA damage. Using the tools of genetic research and bioinformatics, scientists can study this further.

**Data-driven research:** Using bioinformatics tools to analyze large data sets to generate predictions and testable hypotheses.

- *Using bioinformatics tools to analyze large data sets to generate predictions and testable hypotheses is sometimes called **data-driven research**.*

- Now it is time for students to develop their own research questions, while learning about the many ways that people in different careers can use bioinformatics and genetic research. Pass out Student Handout—*Bioinformatics: A Tool for Every Trade* and remind students of the definition of **bioinformatics** found at the top of the handout.
- Assign each group of 2–3 students a number from 1–12 (depending upon class size). Each number corresponds to a different career on the *Student Handout*.
- Ask each student to read the first page of their handout and, while working independently, develop 1–2 research questions that a person in their career might ask. The example of the medical doctor has been filled out for them: *“A Medical Doctor Might Ask... Why does breast cancer seem to affect some families more than others?”*
- After about 5 minutes, tell students to meet with their partner (or other group members) and compare their questions. How are their questions similar? How are they different?
- After about 5 minutes, once all members of the groups have discussed their questions, go around the room and ask each group to share one or more of their research questions. These questions could be written on the board, if desired.
- Once each group has had a chance to share, draw students’ attention to what these questions have in common. These questions will all likely include:
  - Analysis of DNA and/or protein sequences or structures.
  - Use of bioinformatics tools like databases and sequence comparison programs like BLAST.
  - Comparison of one or more groups of organisms or sequences to another.

Students might also note overlaps between the kinds of questions people in different careers might ask. For example, both botanists and marine biologists may study algae found in the oceans, and both marine biologists and conservation biologists may study species impacted by the Gulf Oil Spill of 2010.
- Show **Slide #7**, “DNA Sequencing Core Lab Manager Ellen Sisk”.

Genetic Research: **Slide #7**

**DNA Sequencing Core Lab Manager**  
ELLEN SISK, MS



**Place of Employment:**  
Seattle Biomedical Research Institute

**Type of Work:**  
Manages the DNA Sequencing “Core.” The Core lab is a centralized facility that provides DNA sequencing for all the researchers at the Institute.

The Seattle BioMed Sequencing Core facility has been in operation for over 18 years and offers DNA sequencing and analysis to Seattle’s scientific community, as well as international scientists and organizations. Our service provides cost-effective solutions for small laboratories that lack access to sequencing technology.



16. Pass out copies of Student Handout—*Careers in the Spotlight*.
17. Students should think about, and write down, what kind of work a DNA sequencing core lab manager might do (*Core Lab Manager Question #1*). This will be revisited at the end of the lesson, including how a core lab manager might use bioinformatics in his or her job.
18. Ask students to keep their *Careers in the Spotlight* handout available for future lessons.

## PART II: Genetic Research in Action

19. Pass out Student Handout—*An Introduction to Genetic Research*. Then show students **Slide #8**, which contains pictures of members of the canine family (Canidae): the gray wolf, the coyote, the red fox, and a number of different dog breeds (Canidae): the gray wolf, the coyote, the red fox, and a number of different dog breeds. The slide asks the question, “Which animals are most closely related to one another?”



Genetic Research: **Slide #8**

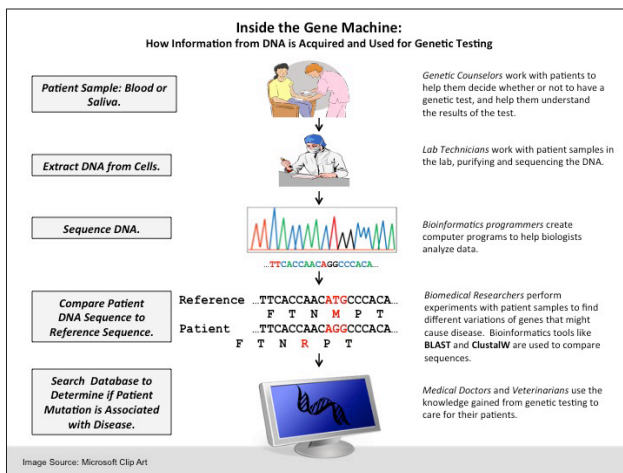
20. Ask students to **develop a hypothesis** and write their hypothesis in *Box #1* on Student Handout—*An Introduction to Genetic Research*. Ask students to **include 3–4 species in their analysis** and explain their reasoning. For example, students may predict that:
  - All of the smaller dog breeds (Jack Russell Terrier, Cocker Spaniel, Toy Poodle) are more closely related than the larger dog breeds (Labradoodle, Newfoundland, English Shepherd). This prediction could be based on the size differences seen in these animals.
  - Given similarities in size and body shapes, the large dogs are more closely related to wolves and/or coyotes than they are to the smaller dogs.
  - Given similarities in habitats and behaviors, the wolves and coyotes are more closely related than wolves and dogs.
21. Ask students, “What kinds of data do we need to answer our questions and test our hypotheses?” The answer is that we need genetic data.

[**Note:** You may wish to show the HHMI video, “Sanger Method of DNA Sequencing,” for students unfamiliar with the process.]

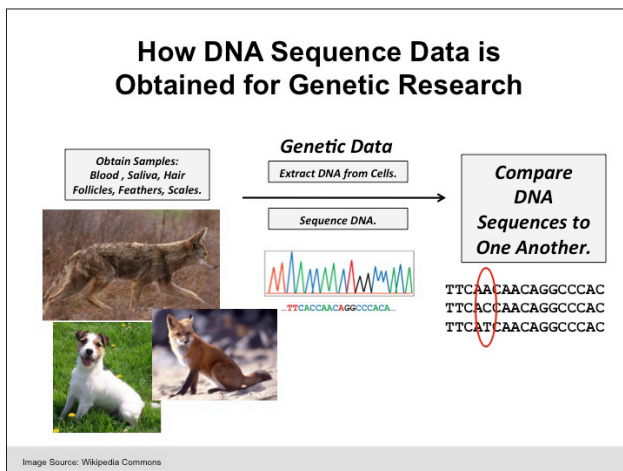
22. Show students **Slide #9**, “Inside the Gene Machine,” which discusses what students learned from the play *Meet the Gene Machine* in the Bio-ITEST Introductory curriculum, *Using Bioinformatics: Genetic Testing*. This includes the following:

- A patient sample is obtained.
- DNA is extracted from the sample.
- DNA is sequenced and analyzed.
- The DNA sequence is compared to known **reference sequences**.
- Databases like the National Center for Biotechnology Information (NCBI) are used to determine whether the patient mutation is associated with cancer.

Genetic Research: **Slide #9**



Genetic Research: **Slide #10**



23. Show students **Slide #10**, “How DNA Sequence Data is Obtained for Genetic Research,” and discuss the similarities between **genetic testing** and **genetic research**:

- Samples are obtained (including samples you don’t see in a hospital or doctor’s office, like feathers or fish scales). Almost any sample that contains cells/DNA can be used.
- DNA is extracted and sequenced. These DNA sequences are the raw data used for analysis in genetic research.

- DNA sequences are compared to one another. In **genetic testing**, a patient's sample is compared to a reference sequence that is known to be free of disease-causing mutations. In the **genetic research** example shown here, we are comparing sequences from dogs and foxes to **one another**; there is no one "correct" or "non-mutated" sequence.

24. Tell students that genetic testing is made possible because of the enormous amount of genetic research that scientists have already done. Genetic research is the first step toward developing tests that can be used in the clinic for genetic testing.
25. Have students look again at their hypotheses from above. Using the information we now have about genetic research, and the "if-and-then" format, we could say, for instance: **If** all of the smaller dog breeds (Jack Russell Terrier, Cocker Spaniel, Toy Poodle) are more closely related than the larger dog breeds (Labradoodle, Newfoundland, English Shepherd), **and** we examine DNA sequence data from each of these dogs, **then** we would expect to find the DNA sequences among the smaller dog breeds to be more similar to each other than they are to the larger dog breeds.
26. Ask students to make any needed changes to their hypothesis in Box #1 on Student Handout—*An Introduction to Genetic Research* to achieve the "if-and-then" format.
27. Pass out the Student Handout—*Canine DNA Sequences* to pairs or groups of three students. Instruct students to cut the sequences into strips so they can be aligned. Teachers may also display **Slide #11**, which shows all of the species that may be analyzed by students.

Genetic Research: **Slide #11**

28. Next, ask students to "align" their DNA sequences. Have students choose sequences included in their hypothesis from Box #1 on Student Handout—*An Introduction to Genetic Research*. Tell students to align the sequences by putting one sequence above the other, with each sequence starting at the same base. Then look for differences between or among the sequences. Once students are happy with their alignment, they can tape their DNA sequences into **Box #2**. They should record the number of differences they find between any pairs of species that were part of their hypothesis.

**Pairwise comparison:** The process of comparing pairs of DNA or protein sequences to one another, to look for similarities and differences between the two sequences. These comparisons can be used to construct a phylogenetic tree.

**Cytochrome c oxidase subunit 1 (COI):** COI is the cytochrome c oxidase subunit 1 gene. COI encodes the COI protein found in the electron transport chain. The entire cytochrome c oxidase protein complex is composed of 13 different protein chains (subunits 1–13). Subunit 1 contains the enzyme's active site. The sequence of cytochrome c oxidase subunit 1 (COI) is similar in all living creatures, and is used for DNA barcoding of animals.

29. Finally, ask students to fill in *Box #3* with their **Results** and **Conclusions** based on their data analysis. What did they learn from their DNA analysis? Was their prediction correct? If not, how would they revise their prediction in light of the new data?

30. Compile the class data set of **pairwise comparisons** of DNA sequences, in which each DNA sequence is compared to the other DNA sequences, one at a time:

- Project the transparency of Teacher Resource—*Pairwise Comparison of Canine DNA Sequences* on the overhead projector. If an overhead projector is not available, a 9 row x 9 column table could be drawn on the board. Alternatively, this *Teacher Resource* could be provided as a *Student Handout*.
- Ask students to help you complete the table, based on their analyses, by calling out the number of nucleotide differences between each pair of species. Start in one corner of the table (gray wolf/red fox) and work your way to the opposite (Toy Poodle/English Shepherd). Write each number in the appropriate cell of the table. When there is disagreement about the correct number of differences, take the answer supplied by the majority of students, or consult Teacher Answer Key—*Pairwise Comparison of Canine DNA Sequences*.
- Based on the number of differences, the class can conclude the following:
  - a. Our data are consistent with the hypothesis that all of the dog breeds and gray wolves are the same species.
  - b. The red fox is the most distantly related among all 8 species.
  - c. The relatedness of the coyote is intermediate between the wolf/dogs and the fox.

31. Show **Slide #12**, “Multiple Sequence Alignment of Canine DNA Sequences.” Tell students that the piece of DNA they analyzed was from a small portion of a gene called **cytochrome c oxidase subunit 1** (also called COI). Bioinformatics is used to analyze long DNA sequences, as shown in this slide, which contains bases 305 to 532 of the COI gene from all of the organisms in this lesson.

Genetic Research: **Slide #12**

### Multiple Sequence Alignment of Canine DNA Sequences

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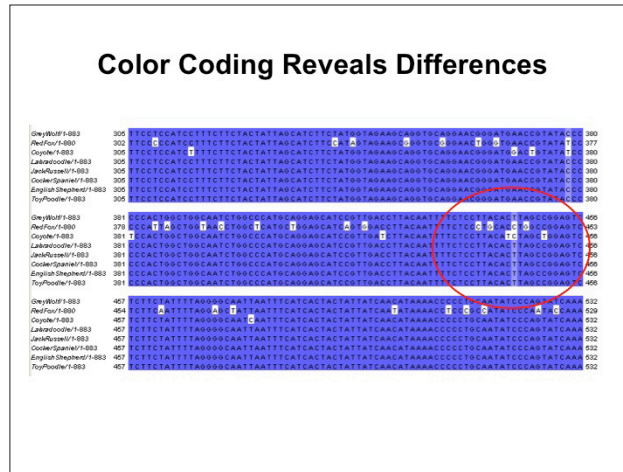
GrayWolf-F-083 305 TTCTCCATCCTTTCTCTACTATTAGCATCTTCTATGATAGAACGAGTGCAGAACGGATGACCGTATATACC 380
RedFox-F-080 305 TTCTCCATCCTTTCTCTACTATTAGCATCTTCTATGATAGAACGAGTGCAGAACGGATGACCGTATATACC 377
Coyote-F-083 305 TTCTCCATCCTTTCTCTACTATTAGCATCTTCTATGATAGAACGAGTGCAGAACGGATGACCGTATATACC 380
Labrador-F-083 305 TTCTCCATCCTTTCTCTACTATTAGCATCTTCTATGATAGAACGAGTGCAGAACGGATGACCGTATATACC 380
Javanese-F-083 305 TTCTCCATCCTTTCTCTACTATTAGCATCTTCTATGATAGAACGAGTGCAGAACGGATGACCGTATATACC 380
Doberman-F-083 305 TTCTCCATCCTTTCTCTACTATTAGCATCTTCTATGATAGAACGAGTGCAGAACGGATGACCGTATATACC 380
EnglishShepherd-F-083 305 TTCTCCATCCTTTCTCTACTATTAGCATCTTCTATGATAGAACGAGTGCAGAACGGATGACCGTATATACC 380
ToyPoodle-F-083 305 TTCTCCATCCTTTCTCTACTATTAGCATCTTCTATGATAGAACGAGTGCAGAACGGATGACCGTATATACC 380

GrayWolf-F-083 381 CCCACTGCTGCAATCTGCGCCATGCGAGGATCCGTTGACCTTACAATTTTCTCTTACACTTACCGGATTC 466
RedFox-F-080 378 CCCATTAGCTAGTACCTGCTGCTGCTGCGAGGATCCGTTGACCTTACAATTTTCTCTTACACTTACCGGATTC 463
Coyote-F-083 381 CCCACTGCTGCAATCTGCGCCATGCGAGGATCCGTTGACCTTACAATTTTCTCTTACACTTACCGGATTC 466
Labrador-F-083 381 CCCACTGCTGCAATCTGCGCCATGCGAGGATCCGTTGACCTTACAATTTTCTCTTACACTTACCGGATTC 466
Javanese-F-083 381 CCCACTGCTGCAATCTGCGCCATGCGAGGATCCGTTGACCTTACAATTTTCTCTTACACTTACCGGATTC 466
Doberman-F-083 381 CCCACTGCTGCAATCTGCGCCATGCGAGGATCCGTTGACCTTACAATTTTCTCTTACACTTACCGGATTC 466
EnglishShepherd-F-083 381 CCCACTGCTGCAATCTGCGCCATGCGAGGATCCGTTGACCTTACAATTTTCTCTTACACTTACCGGATTC 466
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GrayWolf-F-083 467 TCTCTATTTTAAAGGCAATTAATTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCCAATATCAAA 532
RedFox-F-080 464 TCTCTAATTTTAAAGGCAATTAATTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCCAATATCAAA 529
Coyote-F-083 467 TCTCTATTTTAAAGGCAATTAATTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCCAATATCAAA 532
Labrador-F-083 467 TCTCTATTTTAAAGGCAATTAATTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCCAATATCAAA 532
Javanese-F-083 467 TCTCTATTTTAAAGGCAATTAATTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCCAATATCAAA 532
Doberman-F-083 467 TCTCTATTTTAAAGGCAATTAATTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCCAATATCAAA 532
EnglishShepherd-F-083 467 TCTCTATTTTAAAGGCAATTAATTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCCAATATCAAA 532
ToyPoodle-F-083 467 TCTCTATTTTAAAGGCAATTAATTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCCAATATCAAA 532
    
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32. Show **Slide #13**, “Color Coding Reveals Differences,” which presents the same DNA alignment, but color-coded to highlight differences among sequences. **Dark blue** shows regions where all of the sequences are the same, **light blue** show regions where some (but not all) of the sequences are the same, and **white** shows regions of difference. The **red circle** shows the portion of these sequences analyzed by students.

Genetic Research: **Slide #13**



## Closure


33. Summarize today's lesson:
- Students have begun the process of genetic research by generating research questions that people in many different careers might answer using the tools of bioinformatics. They also generated and tested hypotheses about the relatedness of different canines, while learning about some of the types of analyses performed by scientists doing genetic research.
  - In the next lesson (*Lesson Two*), students learn how to identify an unknown DNA sequence using the bioinformatics tool BLAST. They also visit the Barcode of Life Database (BOLD) to learn more about the species from which their DNA sequences were obtained.
  - In subsequent lessons, students will compare DNA sequences to each other and use those comparisons to make inferences about relatedness and evolution (*Lesson Three*). Later lessons will use protein sequences obtained by predicting the amino acid sequences from a sequence of DNA (*Lesson Four*), analyze protein structures (*Lesson Five*), and create a research report about their analyses (*Lesson Six*).
34. Pass out Student Handout—*The Process of Genetic Research* and ask students to fill out the questions for *Lesson One*. Tell students that they will use this handout when they write their Student Research Reports in *Lesson Six*, and they will use it to make a resume at the end of the unit, so they should take good notes. Students could also answer these questions in their lab notebooks, and use that information for their reports and resumes:
- What **did you do** in this lesson?
  - What was your **research question**?

- What was your **hypothesis**?
- Did you **support** or **refute** your hypothesis, or were your results **inconclusive**?
- What **skills** did you learn or practice?

35. Return to the picture of the DNA sequencing core lab manager on **Slide #14**. Review the slide.

Genetic Research: **Slide #14**

**DNA Sequencing Core Lab Manager**  
ELLEN SISK, MS



**Place of Employment:**  
Seattle Biomedical Research Institute

**Type of Work:**  
Manages the DNA Sequencing "Core." The Core lab is a centralized facility that provides DNA sequencing for all the researchers at the Institute.

The Seattle BioMed Sequencing Core facility has been in operation for over 18 years and offers DNA sequencing and analysis to Seattle's scientific community, as well as international scientists and organizations. Our service provides cost-effective solutions for small laboratories that lack access to sequencing technology.

36. Show **Slide #15**, which provides job information for a core lab manager. Review this information with students.

Genetic Research: **Slide #15**

CAREERS IN SPOTLIGHT:  
**DNA Sequencing Core Lab Manager**

**What do they do?**  
The manager oversees the core lab facility. These types of facilities make it possible to perform DNA sequencing reactions and analysis for many different researchers at a given institution, company, or university. The Core lab facility makes it possible for many researchers to share the same DNA sequencing facility and expertise of technicians and the Core Lab Manager.

**What kind of training is involved?**  
Bachelor's degree in biology, molecular biology, biochemistry, or related discipline. Some have a Master's degree or a PhD.

**What is a typical salary for a Core Manager?**  
Salaries vary with experience and range from \$50-\$100,000 per year (\$25-\$50/hour).

Source: Genome Technology Salary Survey 2010

37. Ask students, "What more do we know about a DNA sequencing core lab manager after today's lesson?" Point out that:

- The core lab manager helps many different scientific researchers with their DNA sequencing.
- They perform DNA sequencing, help researchers with DNA sequence data analysis, and provide feedback and share their expertise about DNA sequencing experiments.
- With so many different fields of science using DNA sequence data, many scientists need help obtaining and analyzing DNA sequence data.

36. Ask students to answer Core Lab Manager Question #2 on their *Careers in the Spotlight* handout, which has students explain how this lesson has changed their understanding of what kind of work a core lab manager does.
37. Ask students to also answer *Core Lab Manager Question #3* on their *Careers in the Spotlight* handout, which has students explain how a core lab manager might use bioinformatics in his or her work.
38. Tell students to keep their *Careers in the Spotlight* handout available for future lessons.

## Homework

The following are suggested homework activities to follow this lesson:

- A. Have students read the “The Big Idea: Scanning Life” article from *National Geographic* in preparation for a discussion at the beginning of *Lesson Two*.
- B. Ask students to write about the things they learned in *Lesson One* in their lab notebooks, on another sheet of paper, or in a word processing program like Microsoft® Notepad or Word which they then provide to the teacher as a printout or via email. This can serve as an entry ticket for the following class. Have them complete these prompts:
  - a. Today I learned that...
  - b. An important idea to think about is...
  - c. Something that I don’t completely understand yet is...
  - d. Something that I’m really confident that I understand is...
- C. The *Lesson One* Section of Student Handout—*The Process of Genetic Research* could also be assigned as homework.

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[**Note:** Suggested scoring for homework: +5 points if all four prompts are complete.]

## Glossary

**Bioinformatics:** Bioinformatics is the application of computer science and information technology to biology and medicine. Bioinformatics combines computer science, mathematics, and biology to create methods for capturing, storing, analyzing, visualizing, and sharing biological data. Bioinformatics makes it possible to analyze large quantities of complex biological data and can be used to search biological databases, compare sequences, and draw molecular structures.

**Cytochrome c oxidase subunit 1 (COI):** *COI* is the cytochrome c oxidase subunit 1 gene. *COI* encodes the COI protein found in the electron transport chain. The entire cytochrome c oxidase protein complex is composed of 13 different protein chains (subunits 1–13). Subunit 1 contains the enzyme’s active site. The sequence of cytochrome c oxidase subunit 1 (*COI*) is similar in all living creatures, and is used for DNA barcoding of animals.

**Data-driven research:** Using bioinformatics tools to analyze large data sets in order to generate predictions and testable hypotheses.

**Hypothesis:** A proposed, testable, tentative explanation or relationship for certain facts about the natural world, based on observation.

**Pairwise comparison:** The process of comparing pairs of DNA or protein sequences to one another, to look for similarities and differences between the two sequences. These comparisons can be used to construct a phylogenetic tree.

## Resources

The **Howard Hughes Medical Institute (HHMI)** “Biointeractive” website has a large collection of useful videos and animations on a number of topics, including DNA, evolution, infectious disease, biodiversity, and cancer. These can be freely accessed online at: <http://www.hhmi.org/biointeractive/video/index.html>.

For more information about the **Human Genome Project**, see:

Human Genome Project at: [http://en.wikipedia.org/wiki/Human\\_Genome\\_Project](http://en.wikipedia.org/wiki/Human_Genome_Project).

National Human Genome Research Project’s *The Human Genome Project Completion: Frequently Asked Questions*. Available at: <http://www.genome.gov/11006943>.

Chial, H. DNA sequencing technologies key to the Human Genome Project. *Nature Education*. 2008; 1: 1.

For more information about the **data-driven nature of science** today, as well as the role of large data sets in hypothesis and prediction, see the following articles:

Smalheiser, N.R. Informatics and hypothesis-driven research. *EMBO Reports*. 2002; 3: 702.

Sanders, N. (2006). *Data-driven research*. Available at: <http://nsaunders.wordpress.com/2006/09/29/data-driven-research/>.

Kell, D.B. and Oliver, S.G. Here is the evidence, now what is the hypothesis? The complementary roles of inductive and hypothesis-driven science in the post-genomic era. *BioEssays*. 2003; 26: 299.

For more information about **dogs and dog genetics**, see:

The one-hour NOVA program *Dogs and More Dogs* presents the story of dogs and how they evolved into the diverse breeds we see today. PBS has developed a *Dogs and More Dogs* companion website which contains links to the online video, as well as a Teachers’ Guide and other related resources. Available here: <http://www.pbs.org/wgbh/nova/dogs/>.

The one-hour NOVA program *Dogs Decoded* further explores the evolution of dogs, the possible mechanisms of their domestication, and what recent genetic analyses have revealed. The video can be purchased through the PBS website at: <http://www.pbs.org/wgbh/nova/nature/dogs-decoded.html>.

## Credit

National Human Genome Research Project. *The Human Genome Project Completion: Frequently Asked Questions*. Accessed November 18, 2011 from: <http://www.genome.gov/11006943>.

Sanders, N. (2006). Data-driven research. Accessed November 18, 2011 from: <http://nsaunders.wordpress.com/2006/09/29/data-driven-research/>.

Sisk, Ellen. Personal Interview. 26 July 2010.

The authors wish to thank Wikimedia Commons and Microsoft® Clipart for many of the images found in the PowerPoint slides associated with this lesson.



**1**

**Pairwise Comparisons  
of Canine DNA Sequences**

	Gray wolf	Red fox	Coyote	Labra-doodle	Jack Russell	Cocker Spaniel	English Shepherd	Toy Poodle
Gray wolf								
Red fox								
Coyote								
Labra-doodle								
Jack Russell								
Cocker Spaniel								
English Shepherd								
Toy Poodle								



Name \_\_\_\_\_ Date \_\_\_\_\_ Period \_\_\_\_\_

## 1

## Bioinformatics: A Tool for Every Trade

### What is Bioinformatics?

Bioinformatics is the application of computer science and information technology to biology and medicine. Bioinformatics combines **computer science, mathematics, and biology** to create methods for capturing, storing, analyzing, visualizing, and sharing biological data. Bioinformatics makes it possible to analyze large quantities of complex biological data and can be used to **search biological databases, compare sequences, and draw molecular structures**.

### Student Researcher Background:

Over the past few decades, major advances in both biology and computer technology have led to an explosive growth in the genetic information generated by the scientific community. The massive amount of information has, in turn, led to the development of computerized databases and specialized tools, like those found at the National Center for Biotechnology Information (NCBI). The databases are used to store, organize, and index the data; the specialized tools are used to view and analyze the data. The ultimate goal of bioinformatics is to facilitate new biological discoveries as well as to create a global perspective from which unifying principles in biology can be understood. Scientists in many different fields can use the fruits of bioinformatics to further their research, help treat patients, and preserve our natural environment.

**Aim:** Today, your job as a researcher is to:



1. Write a research question that you think someone in your assigned career might ask.
2. Meet with your partner and compare research questions. How are they similar? How are they different?
3. Share your research questions with your teacher and classmates during a group discussion.

*The medical doctor's question has been filled out for you, with the example you learned about in the bioinformatics unit on genetic testing.*

### Example:

#### A Medical Doctor Might Ask...

Why does breast cancer seem to affect some families more than others?

Medical doctors now understand why some people have an increased risk of breast cancer, thanks to the work of human geneticist Mary-Claire King, PhD. Now a professor at the University of Washington, in 1990 Dr. King discovered a single gene on chromosome 17 that was responsible for inheritance of an increased risk of breast cancer (Hall et al. *Science* 1990). This gene was later named *BRCA1*, for "breast cancer, early onset." Both *BRCA1* and *BRCA2* (which encodes a related protein) are involved in repairing DNA damage. A number of different mutations have been described that alter or abolish the function of these proteins, and people who inherit mutated forms of either *BRCA1* or *BRCA2* have a greatly increased risk of cancer. Together, mutations in these two genes account for 5–10% of all cases of breast cancer.

### **1. A Genetic Counselor Might Ask...**

*Genetic counselors are specially trained to help people understand their genetic risk for different conditions, educate them about the diseases or conditions, and assess the risk of passing the diseases or conditions onto their children.*

### **2. A Fish and Wildlife Service Forensic Scientist Might Ask...**

*The US Fish & Wildlife Service Forensics Laboratory in Ashland, Oregon is the only lab in the world dedicated to crimes against wildlife. Their crime lab is very much like a "typical" police lab, except the victim is an animal. The scientists examine, identify, and compare evidence to link the suspect(s), victim(s), and crime scene with physical evidence.*

### **3. A Veterinarian Might Ask...**

*Genetic testing is no longer just for humans! Many genetic tests are now available for animals, including tests for hypertrophic cardiomyopathy, the most common form of heart disease in cats.*

### **4. A Computer Scientist Might Ask...**

*Computer scientists help develop the tools and databases used in bioinformatics, like those found at the National Center for Biotechnology Information (NCBI), including the Nucleotide and Protein databases at the NCBI and the sequence alignment tool BLAST. Without computer scientists, biologists would have a difficult time cataloging and analyzing all the data they generate.*

**5. An Ecologist Might Ask...**

*Ecologists study the relationships between organisms and their environment, including the distribution of different species, the relationships between plants and animals, and how one species affects another.*

**6. A Conservation Biologist Might Ask...**

*Conservation biologists study the nature and status of ecosystems, with the goal of protecting species, their habitats, and entire ecosystems from extinction. This often involves managing natural resources.*

**7. An Evolutionary Biologist Might Ask...**

*Evolutionary biologists study the origin of species, including their descent from other species or a common ancestor, as well as how species change, multiply, and diversify over time.*

**8. A Marine Biologist Might Ask...**

*Marine biologists study organisms that live in or near the oceans, including mammals, fish, seaweed, and plankton. Oceans comprise over 71% of the Earth's surface and contain a large proportion of all life on Earth.*

### 9. A Botanist Might Ask...

*Botanists study all plant life and their structure, growth, reproduction, metabolism, diseases, and evolutionary history. Botanists also identify new plant species.*

### 10. A Microbiologist Might Ask...

*Microbiologists study microscopic, unicellular organisms such as fungi, protists, bacteria and viruses—all things that are too small to see without a microscope. It is estimated that only about one percent of all of the microbe species on earth have been studied so far.*

### 11. A Toxicologist Might Ask...

*Toxicologists study how chemicals like poisons affect living organisms. They study the symptoms, mechanisms, treatment, and detection of poisoning of humans, other animals, and plants.*

### 12. An Epidemiologist Might Ask...

*"Epidemiologist" comes from the same root word as "epidemic," meaning "on or in people." They study the factors affecting the health and illness of populations, including infectious diseases. They are a vital part of public health and preventive medicine.*

To learn more about bioinformatics, visit: <http://www.ncbi.nlm.nih.gov/About/primer/bioinformatics.html>

To learn more about each of the careers above, visit the Bio-ITEST Careers Site at: <http://www.nwabr.org/students/student-resource-center/career-center>

Name \_\_\_\_\_ Date \_\_\_\_\_ Period \_\_\_\_\_

# 1

## Careers in the Spotlight

### What is Bioinformatics?

Bioinformatics is the application of computer science and information technology to biology and medicine. Bioinformatics combines **computer science, mathematics, and biology** to create methods for capturing, storing, analyzing, visualizing, and sharing biological data. Bioinformatics makes it possible to analyze large quantities of complex biological data and can be used to **search biological databases, compare sequences, and draw molecular structures**.

#### Lesson One Career: Core Lab Manager

Ellen Sisk

1. What kind of work do you think a **core lab manager** does?

2. How has this lesson changed your understanding of the kind of work a **core lab manager** does?

3. How do you think a **core lab manager** might use or benefit from bioinformatics?

#### Lesson Two Career: Postdoctoral Fellow in DNA and History

Krishna Veeramah, PhD

1. What kind of work do you think a person studying **DNA and History** does?

2. How has this lesson changed your understanding of the kind of work a person studying **DNA and History** does?

3. How do you think a person studying **DNA and History** might use or benefit from bioinformatics?

<p><b>Lesson Three Career: Microbiologist</b> Lalita Ramakrishnan, PhD</p>	
<p>1. What kind of work do you think a <b>microbiologist</b> does?</p>	<p>2. How has this lesson changed your understanding of the kind of work a <b>microbiologist</b> does?</p> <p>3. How do you think a <b>microbiologist</b> might use or benefit from bioinformatics?</p>
<p><b>Lesson Four Career: Biological Anthropologist</b> Michael Crawford, PhD</p>	
<p>1. What kind of work do you think a <b>biological anthropologist</b> does?</p>	<p>2. How has this lesson changed your understanding of the kind of work a <b>biological anthropologist</b> does?</p> <p>3. How do you think a <b>biological anthropologist</b> might use or benefit from bioinformatics?</p>
<p><b>Lesson Five Career: Molecular Diagnostics Researcher</b> James Ferrenberg</p>	
<p>1. What kind of work do you think a <b>molecular diagnostics</b> researcher does?</p>	<p>2. How has this lesson changed your understanding of the kind of work a <b>molecular diagnostics researcher</b> does?</p> <p>3. How do you think a <b>molecular diagnostics researcher</b> might use or benefit from bioinformatics?</p>



<p><b>Lesson Six Career: Science and Technical Writer</b> Kris Freeman</p>	
<p>1. What kind of work do you think a <b>science and technical writer</b> does?</p>	<p>2. How has this lesson changed your understanding of the kind of work a <b>science and technical writer</b> does?</p> <p>3. How do you think a <b>science and technical writer</b> might use or benefit from bioinformatics?</p>
<p><b>Lesson Seven Career: Pediatric Neurologist</b> Russell Saneto, DO, PhD</p>	
<p>1. What kind of work do you think a <b>pediatric neurologist</b> does?</p>	<p>2. How has this lesson changed your understanding of the kind of work a <b>pediatric neurologist</b> does?</p> <p>3. How do you think a <b>pediatric neurologist</b> might use or benefit from bioinformatics?</p>

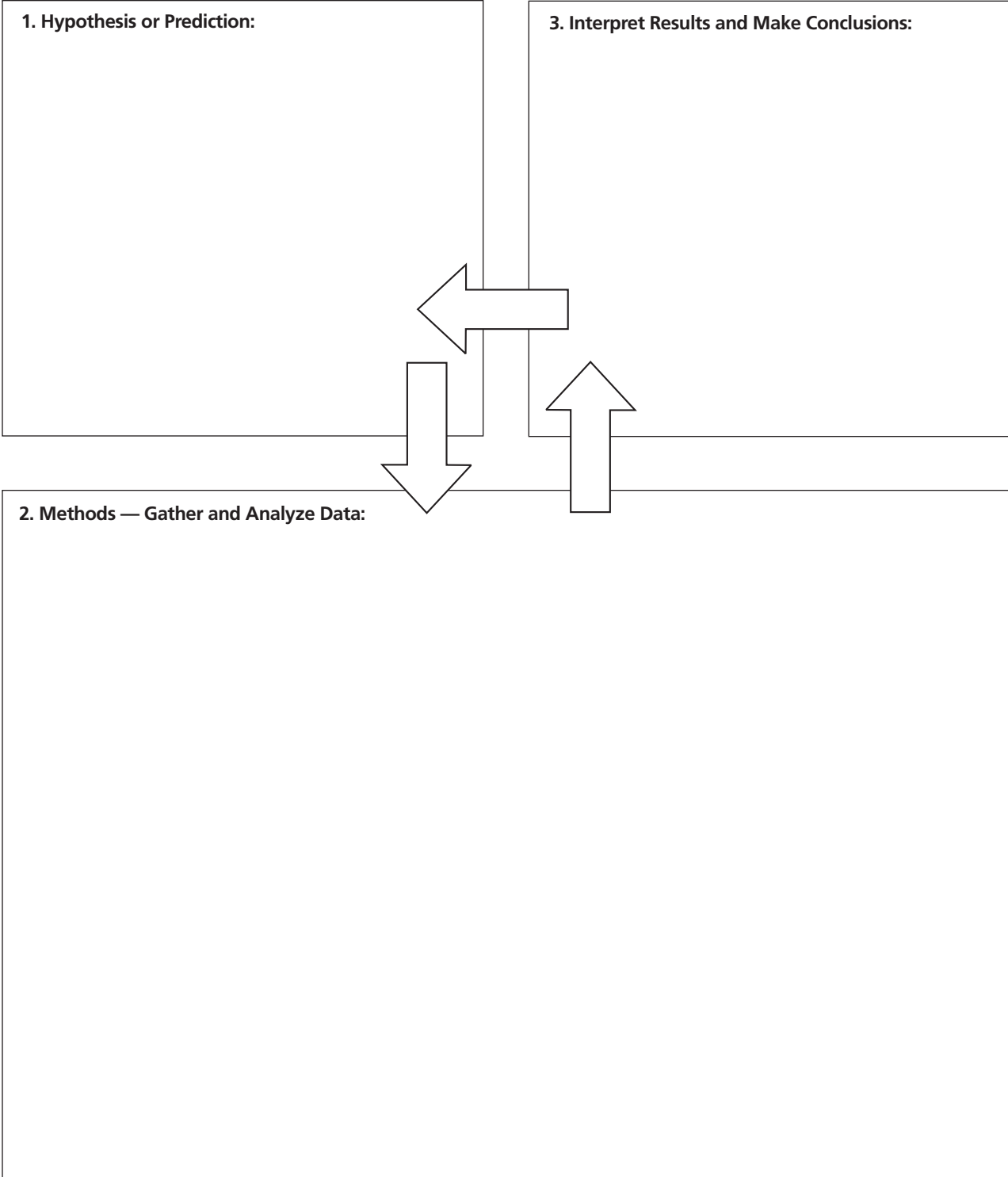
# LESSON 1

## HANDOUT

Name \_\_\_\_\_ Date \_\_\_\_\_ Period \_\_\_\_\_

**1**

**An Introduction to Genetic Research**



**1**

**Canine DNA Sequences**

Gray wolf	CTTACACTTAGCCGGAGT
Red fox	CCTGCACCTGGCCGGAGT
Coyote	CTTACATCTAGCTGGAGT
Labradoodle	CTTACACTTAGCCGGAGT
Jack Russell	CTTACACTTAGCCGGAGT
Cocker Spaniel	CTTACACTTAGCCGGAGT
English Shepherd	CTTACACTTAGCCGGAGT
Toy Poodle	CTTACACTTAGCCGGAGT

Name \_\_\_\_\_ Date \_\_\_\_\_ Period \_\_\_\_\_

# 1

## The Process of Genetic Research

### Student Researcher Background:

This handout is designed to help you summarize the steps involved in performing your genetic research and to help you prepare for writing your Student Research Report and your resume at the end of this unit. Your teacher may ask you to hand in this sheet with your answers throughout the unit, or you may be instructed to keep it with you to help you remember the steps involved and the tools you used. Answer the questions as you work through each lesson, and write down notes that will help you remember what you have done and why.

### Lesson One: The Process of Genetic Research

What **did you do** in this lesson?

What was your **Research Question** about the canines?

What was your **Hypothesis** about the relatedness of the canines?

Did you **support** or **refute** your hypothesis, or were your results **inconclusive**?

What **skills** did you learn or practice?

### Lesson Two: DNA Barcoding and the Barcode of Life Project

What **did you do** in this lesson?

**Methods:** What bioinformatics program(s) or database(s) did you use?

**Results & Conclusions:** What did you find? What could you conclude from your analysis?

What **skills** did you learn or practice?

What is your **hypothesis** about the relatedness of the species within your group (*Question #23 from Student Handout—Using BLAST and BOLD for Genetic Research*)?

### **Lesson Three: Using Bioinformatics to Study Evolutionary Relationships**

What **did you do** in this lesson?

**Methods:** What bioinformatics program(s) or database(s) did you use?

**Results & Conclusions:** What did you find? What could you conclude from your analysis?

What **skills** did you learn or practice?

### **Lesson Four: Using Bioinformatics to Analyze Protein Sequences**

What **did you do** in this lesson?

**Methods:** What bioinformatics program(s) or database(s) did you use?

**Results & Conclusions:** What did you find? What could you conclude from your analysis?

What **skills** did you learn or practice?

### **Lesson Five: Protein Structure Dictates Function**

What **did you do** in this lesson?

**Methods:** What bioinformatics program(s) or database(s) did you use?

**Results & Conclusions:** What did you find? What could you conclude from your analysis?

What **skills** did you learn or practice?

## 1

## Bioinformatics: A Tool for Every Trade Teacher Answer Key

**1. A Genetic Counselor Might Ask...**

Answers vary. Potential answers include:

- Why does one group of people or one family suffer from a particular disease or condition while others do not?
- Does a disease result from a genetic condition, the environment, or both?

**2. A Fish and Wildlife Service Forensic Scientist Might Ask...**

Answers vary. Potential answers include:

- Is a particular fish endangered or protected (for example, salmon)?
- Is a particular sample of meat from an animal that was hunted illegally?

**3. A Veterinarian Might Ask...**

Answers vary. Potential answers include:

- Is a disease or condition in cats [or dogs] genetic, environmental, or both?
- Does this breed of dog have a genetic susceptibility to a given disease?
- Does a family or line of dogs suffer from a genetic susceptibility to a given disease?

**4. A Computer Scientist Might Ask...**

Answers vary. Potential answers include:

- How can we make a new computer program for aligning DNA sequences?
- How can we improve the current programs for aligning DNA sequences?
- Can we create a database about genetic diseases and genetic testing that is useful to the public?

**5. An Ecologist Might Ask...**

Answers vary. Potential answers include:

- Is the species of salmon in stream A the same species of salmon found in stream B?
- How has the 2010 Gulf Oil Spill affected the distribution of marine mammals?

**6. A Conservation Biologist Might Ask...**

Answers vary. Potential answers include:

- What larval species have died as a result of the 2010 Gulf Oil Spill? Are those species endangered or threatened?
- Are the sea lions found off the coast of Washington the same species as the sea lions found off the coast of California?

**7. An Evolutionary Biologist Might Ask...**

Answers vary. Potential answers include:

- How long ago did the monkeys of the New World diverge from the monkeys of the Old World?  
What was the common ancestor for New World and Old World monkeys?
- What is the closest living relative of *Tyrannosaurus rex*?

**8. A Marine Biologist Might Ask...**

Answers vary. Potential answers include:

- How many different species of sea birds have been found in coastal areas impacted by the 2010 Gulf Oil Spill?
- Has the distribution of sea plants changed in the past 20 years, as ocean temperatures have risen?

**9. A Botanist Might Ask...**

Answers vary. Potential answers include:

- What varieties of wheat are most resistant to fungal diseases, and what are the genes that are responsible for this resistance?
- Where did invasive weeds originate, such as the star thistle found in California?

**10. A Microbiologist Might Ask...**

Answers vary. Potential answers include:

- Is the antibiotic resistance found in a particular group of bacteria caused by the same gene?
- How many species of bacteria are found on the average drinking fountain?

**11. A Toxicologist Might Ask...**

Answers vary. Potential answers include:

- Are some people's bodies better able to break down certain environmental toxicants, and if so, what genes are responsible for this?
- How do carcinogens or chemicals cause cancer?

**12. An Epidemiologist Might Ask...**

Answers vary. Potential answers include:

- Is the latest outbreak of influenza caused by H1N1 ("bird flu")?
- Where did the Human Immunodeficiency Virus (HIV) originate and when?



1

# An Introduction to Genetic Research

## Teacher Answer Key

[Note: The suggested total point value for this worksheet is **15 points**, or approximately 5 points per question.]

**1. Hypothesis or Prediction:**

*Answers vary. Potential answers would resemble the following, including 3–4 species in the hypothesis and analysis below:*

*Larger dogs like Labradoodles and English Shepherds are more closely related to coyotes than to wolves or small dogs like Toy Poodles.*

**3. Interpret Results and Make Conclusions:**

*Answers vary, but should be based on the hypothesis (Box 1) and the Analysis (Box 2), such as:*

*I originally thought that larger dogs were more closely related to coyotes than to small dogs, but actually all the dogs have the same DNA sequences and the coyote is different.*

**2. Methods — Gather and Analyze Data:**

*Answers vary, but will include DNA strips aligned and taped in place as shown below, with any DNA base differences circled or otherwise noted.*

<b>Coyote</b>	CTTACATCTAGCTGGAGT
<b>Labradoodle</b>	CTTACACTTAGCCGGAGT
<b>English Shepherd</b>	CTTACACTTAGCCGGAGT
<b>Toy Poodle</b>	CTTACACTTAGCCGGAGT

## 1

## The Process of Genetic Research Teacher Answer Key

[**Note:** The suggested total point value for this worksheet is **25 points**, with **5 points possible for each set of lesson questions** (i.e., 1 point per question). For *Lessons Three, Four, and Five*, greater weight may be given to the “Results & Conclusions” questions (i.e., 2 points each).]

This handout is designed to help students prepare and organize their activities for the Student Research Reports they will prepare in *Lesson Six* and the resumes they will prepare in *Lesson Eight*. It could also be turned in throughout the unit to serve as a formative assessment. The answers provided here are sample student answers; actual answers are expected to vary.

### Lesson One: The Process of Genetic Research

What **did you do** in this lesson?

- *Overview of the process of genetic research, methods, and research questions.*
- *Learned how to develop research questions and hypotheses.*

What was your **Research Question** about the canines?

*Are domestic dogs more closely related to wolves or foxes?*

What was your **Hypothesis** about the relatedness of the canines?

*Dogs and wolves are more closely related than dogs and foxes.*

Did you **support** or **refute** your hypothesis, or were your results **inconclusive**?

*Supported—dogs and wolves are the same species.*

What **skills** did you learn or practice?

- *Generating hypotheses.*
- *Aligning and comparing DNA sequences.*
- *Using data to evaluate hypotheses.*

**Lesson Two: DNA Barcoding and the Barcode of Life Project**

What **did you do** in this lesson?

- Identified an unknown DNA sample using BLAST.
- Found taxonomic information about my species at the Barcode of Life Database (BOLD).
- Used the taxonomic information to form a scientific collaboration and generate a research hypothesis.

**Methods:** What bioinformatics program(s) or database(s) did you use?

*BLAST and the Barcode of Life Data System (BOLD).*

**Results & Conclusions:** What did you find? What could you conclude from your analysis?

*Students will have identified the species that served as the source of their barcode sequence. They will also form a group with other students who have barcode sequences from related species.*

What **skills** did you learn or practice?

- Identifying an unknown DNA sequence using BLAST.
- Obtaining taxonomic information from the Barcode of Life Database.
- Collaborating with other student scientists.

What is your **hypothesis** about the relatedness of the species within your group (Question #23 from Student Handout—Using BLAST and BOLD for Genetic Research)?

*This will vary by group, but will be based on the research questions provided.*

**Lesson Three: Using Bioinformatics to Study Evolutionary Relationships**

What **did you do** in this lesson?

- Aligned DNA sequences to see where they are the same and where they differ.
- Used this alignment to make a phylogenetic tree and evaluate evolutionary relationships.

**Methods:** What bioinformatics program(s) or database(s) did you use?

*ClustalW and JalView, BLAST.*

**Results & Conclusions:** What did you find? What could you conclude from your analysis?

*Students should have found some differences among the DNA sequences in their group and made conclusions about the relatedness of these species based on that analysis. Students should relate their conclusions to their original hypothesis about species relatedness.*

What **skills** did you learn or practice?

- Aligning and comparing DNA sequences using ClustalW and JalView.
- Constructing a phylogenetic tree using BLAST.
- Analyzing genetic data to assess my hypothesis.

**Lesson Four: Using Bioinformatics to Analyze Protein Sequences**

What **did you do** in this lesson?

*Predicted the protein sequence from the DNA sequence and identified which reading frame is correct (i.e., which one makes a functional protein).*

**Methods:** What bioinformatics program(s) or database(s) did you use?

*ORFinder, BLAST.*

**Results & Conclusions:** What did you find? What could you conclude from your analysis?

*DNA sequences seem to encode many possible proteins, but only one reading frame tends to yield the correct protein sequence. Students should come to the same basic conclusions about the relatedness of the species in their group as they did in Lesson Three above.*

What **skills** did you learn or practice?

- *Identifying all six reading frames within a given DNA sequence.*
- *Choosing the correct open reading frame within a given DNA sequence.*
- *Collaborating with other student scientists.*

**Lesson Five: Protein Structure Dictates Function**

What **did you do** in this lesson?

*Viewed and manipulated the structures of COI (wild type and those containing a poison).*

**Methods:** What bioinformatics program(s) or database(s) did you use?

*NCBI Structure database and Cn3D.*

**Results & Conclusions:** What did you find? What could you conclude from your analysis?

*Students should be able to conclude that the area most vital to protein function is the active site.*

What **skills** did you learn or practice?

- *Viewing protein structures in Cn3D.*
- *Identifying the active site.*
- *Collaborating with other student scientists.*

**1**

**Pairwise Comparisons of Canine DNA Sequences Teacher Answer Key**

	Gray wolf	Red fox	Coyote	Labradoodle	Jack Russell	Cocker Spaniel	English Shepherd	Toy Poodle
Gray wolf								
Red fox	4							
Coyote	3	5						
Labradoodle	0	4	3					
Jack Russell	0	4	3	0				
Cocker Spaniel	0	4	3	0	0			
English Shepherd	0	4	3	0	0	0		
Toy Poodle	0	4	3	0	0	0	0	

# LESSON 1

## KEY