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TEACHING THE GENOME GENERATION

Ancestry Testing

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Contents

Ancestry Testing Module Overview

Introduction & Theme

This module aims to introduce students to the concept of ancestry DNA testing, using a narrative to frame the learning activities. Students will follow the fictional story of Sam, a high school student who wants an at-home ancestry DNA test for their 18th birthday. Each activity will begin with a scene from Sam's life:

> In Part 1, Sam discusses wanting an ancestry test kit for their birthday, and students familiarize themselves with ancestry tests and consider different "case study" scenarios about potential test results. In Part 2, Sam learns about how ancestry testing works, and students perform calculations to generate allele count and frequency data and compare DNA sequence data.
>
> *Parts 3-5 are still in development and will be released as additional activities when available. Part 3 continues Sam's learning, and students discover how human migration patterns influenced variant allele frequencies across populations. In Part 4, students learn about the connections between ancestry and human health, exploring databases and performing calculations for variants with known phenotypes (TtGG genes). Finally, Part 5 finds Sam contemplating whether to take the test, and students are asked to debate and finish Sam's story.*

In addition to the biology concepts introduced, students will use quantitative skills to calculate DNA variations in individuals and across populations. They will also interpret and explain results, such as associating individuals with geographic populations.

Each part of the Ancestry Testing module also includes accompanying sections on bioethics and career exploration that are included as parts of the main activity, and can be added to the activity or used separately. In each Ethics section, students will connect social and cultural themes to the biology concepts in the activity through research, reflections, predictions, discussions, and/or debates. In each Careers section, students will perform self-directed exploration of jobs associated with the learning topics they just learned about in the main activity.

Learning Outcomes

Essential Questions

- How does ancestry testing work?
- Why do ancestry test results change?
- What do ancestry test results mean, for me, for my family, for my health?
- How does my ancestral DNA information connect with my identity?

Enduring Understandings

- DNA is inherited (and lost) across generations, such that not all genealogical ancestors are genetic ancestors.
- Ancestry testing typically involves sequencing of genomic single nucleotide variants.
- Reference genomes for ancestry tests are comprised of aggregate single nucleotide variant data from varying numbers of individuals.
- Ancestry information can inform about personal and family history and health outcomes.

Skills

Data table usage and interpretation; computation (math skills); asking questions and formulating hypotheses; problem solving; pattern recognition; constructing explanations; reading comprehension.

Lesson Descriptions & Learning Objectives

Activity 1: Introduction to Ancestry Testing

Description

Sam discusses wanting an ancestry test kit for their birthday, and students familiarize themselves with ancestry testing companies and the features that are offered from this type of test. Students also explore real scenarios from individuals have taken ancestry tests, and reflect on different "case study" scenarios. Finally, students explore careers that relate to the themes of this activity.

Skills	• Reading comprehension • Asking questions and formulating hypotheses • Constructing explanations
Concepts	• Genetic testing • Ancestry testing • Genetic data and privacy
Learning Objectives	• Genetic testing can inform about personal and family history, as well as health outcomes
	• Unexpected information can be revealed from genetic tests that affect the individual and their family
	• A variety of career paths relate to this activity

Activity 2: Sequence Comparison in Ancestry Testing

Description

Sam learns about how ancestry testing works, and students perform calculations to generate allele count and frequency data and compare DNA sequence data. Students also consider how human populations are defined as groups, geographically and over time. Finally, students explore careers that relate to the themes of this activity.

Skills	• Data table usage and interpretation • Spreadsheet usage • Computation (math skills) • Asking questions and formulating hypotheses • Problem solving • Pattern recognition • Constructing explanations
Concepts	• Basic principles of inheritance • Genetic variation and single nucleotide variants • Allele frequencies • Tables and spreadsheets
Learning Objectives	• Ancestry testing typically involves sequencing of single nucleotide variants
	• Ancestry reference genomes are aggregate single nucleotide variant data from varying numbers of individuals
	• Allele frequencies represent the proportion of each allele at a DNA site in a population
	• Population descriptors do not neatly fit in geographic categories
	• A variety of career paths relate to this activity

Lessons & Activities

Activity 1: Introduction to Ancestry Testing

Sam's Story: What is ancestry testing?

Sam is a high school student who is about to turn 18 years old. They are at home with their Grandma and cousin Tan. Grandma reveals that the family wants to all contribute to buy Sam a present to celebrate this big milestone birthday. Sam shares that they want a DNA ancestry test for their birthday gift, but gets an unexpected reaction from Grandma.

Read the scene below from Sam's life. If you're in a class or group, assign one person as Sam, one person as Tan, and one person as Grandma, and read the scene out loud.

> ***Tan:*** *Happy 18th birthday, Sam! I can't believe you're an adult now. You're so OLD!*
>
> ***Grandma:*** *It feels like just yesterday we were waiting for your arrival in the hospital, Sam. Ah, how time flies!*
>
> ***Tan:*** *Grandma, tell Sam about the gift idea!*
>
> ***Grandma:*** *Right. Sam, this is a big birthday, so the family wants to come together and all chip in to buy you something special. What would you like as a birthday gift?*
>
> ***Sam:*** *Oh, I know exactly what I want! I'm finally old enough, so I want one of those ancestry DNA test kits!*
>
> ***Tan:*** *An-ses-tree? What's that??*
>
> ***Sam:*** *Haven't you seen those commercials? You just spit in a tube and send off your DNA and find out where you're from in the world! It even tells you about your health, like what diseases you'll get!*
>
> ***Tan:*** *SO cool! I can't wait to take one when I'm old enough! I want to know all about MY own DNA!*
>
> ***Sam:*** *What's wrong, Grandma? Aren't you excited to learn more about our family's roots?*
>
> ***Grandma:*** *Oh, Sam. We know enough about where our family is from. What's this test going to tell us that we don't already know? And sending your DNA off to a company like that? I just don't like this idea…*

Prediction

Sam wants an ancestry test for their 18th birthday. List 2 reasons why someone would want to take an ancestry test.

1.

2.

Grandma has concerns about the ancestry test. List 2 reasons why someone would not want to take an ancestry test.

1.

2.

Sam and Tan talk about being old enough to take an ancestry test. Why might there be age restrictions on DNA ancestry tests?

Background

Sam shares with their family that they want a DNA ancestry test for their 18th birthday, and is surprised to find that Grandma and cousin Tan have different feelings about it. Familiarize yourself with this type of genetic test, it's purpose and how it works, as well as important considerations about privacy and genetic data sharing.

Genetics & Inheritance

When someone talks about their personal genetics, they are often referring to aspects of their own **DNA** and **genome**. The human genome is the complete set of DNA in an individual that encodes the instructions for making each of us who we are. Where does this DNA come from? Typically, each person has two biological parents, four grandparents, eight great-grandparents, etc. as shown in the **pedigree** in Figure 1. Each of these biological ancestors can contribute DNA to the individual. Individuals inherit half of their DNA from each of their two biological parents, one quarter of their DNA from their four biological grandparents, one eighth of their DNA from their eight great-grandparents, and so on. Therefore, individuals are a mix of DNA from their ancestors; biologically related individuals often share some of the same DNA.

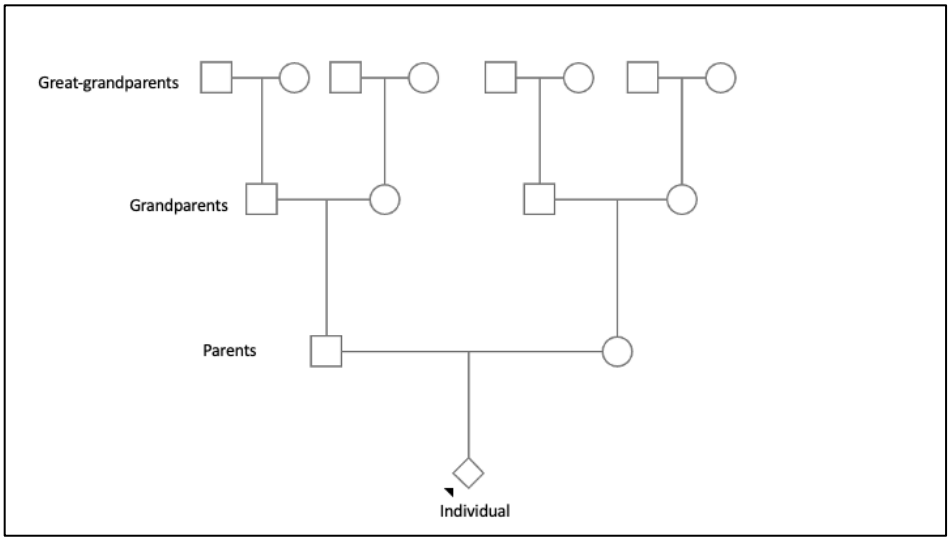


Figure 1. In this pedigree, or family tree, an individual is shown at the bottom. Going up the tree reveals some of their biological ancestors: parents, grandparents, and great-grandparents.

Genetic Testing

Genetic testing is a category of laboratory tests that examines an individual's genes or other biological factors that influence genetic functions and traits. A small sample of cells, typically from blood or saliva, is taken from an individual and DNA, **RNA**, and/or **protein** molecules are examined. The goal of genetic testing is to better understand a person's DNA features, RNA patterns, or protein levels and how they influence a person's health, traits, or genetic heritage. Many types of genetic tests have been developed for a variety of purposes, including **karyotype** tests that count the number of **chromosomes** per cell to look for genetic conditions such as trisomy 21 (Down Syndrome); **tumor** tests that examine tumor cells to

determine drivers of and treatments for cancer; and paternity tests that reveal an individual's biological relatives.

Most genetic tests are conducted through healthcare professionals like doctors; these types of tests are called **clinical genetic tests**. Doctors often determine a test is needed due to a specific medical reason, such as a family history of a genetic disorder or symptoms that suggest a genetic condition. Samples like blood or saliva are collected in a medical setting and analyzed in a clinical laboratory. Once the test is complete, the results are sent to the healthcare professional who then shares them with the individual. With clinical genetic tests, health insurance may cover some or all of the cost of the test.

In contrast, **direct-to-consumer genetic tests** are tests that can be purchased directly by people without a doctor's order. They are often advertised as a way to learn about your ancestry, genetic traits, or health risks directly from your DNA. Individuals choose what test they want performed, and collect and send their own samples to the testing company. The testing company analyzes the samples, and once the test is complete the results are sent directly to the individual. With direct-to-consumer genetic tests, the individual pays for all of the cost of the test.

Thought questions:

Have you ever had a test performed at the doctor's office? Was it a genetic test?

Have you seen advertisements for direct-to-consumer genetic tests? What information would the test reveal?

Ancestry Testing

DNA **ancestry tests**, or genealogical DNA tests, are a type of direct-to-consumer genetic test that examines specific locations in an individual's DNA to find similarities between groups of people and predict their ancestral origins. Since DNA is passed from biological parents to their offspring, it is possible to trace genetic ancestors by examining a person's DNA. This process relies on comparing an individual's DNA to reference databases containing genetic information from populations of people worldwide. Each company uses a different approach to for the ancestry test, and may offer additional features such as health reports and family matching.

Ancestry testing has gained popularity in recent years due to its ability to uncover previously unknown family connections, shed light on migration patterns, and help individuals better understand their roots and cultural identities.

Genetic Information & Privacy

Genetic tests offer valuable insights into in individual's genetic makeup, and can advance understanding of a person's ancestry, disease predisposition, and personalized medical treatments. However, they also raise profound concerns about privacy and ethical implications of sharing one's most intimate biological data. Since DNA is inherited, one person's genetic test results may reveal information about other biological relatives. The sharing of genetic data can expose individuals and families to risks such as genetic discrimination, breaches of confidentiality, and unauthorized access to sensitive information.

In the United States, the Genetic Information Nondiscrimination Act (GINA) provides protection for genetic information. This federal law protects the confidentiality of genetic information, and orders that genetic information be part of a person's confidential medical record to be stored and shared under strict privacy standards. GINA also specifically protects against discrimination based on genetic information for health insurance and employment. GINA prohibits health insurance companies from using genetic information to alter a person's health insurance benefits. This law also prohibits employers from making decisions about hiring, firing, or promotions based on genetic information.

Thought question:

GINA protects genetic information specifically regarding health insurance and employment. In what other contexts might genetic information privacy be relevant?

Quick Knowledge Check

Check your understanding of the background material by answering these questions.

1. List two types of genetic tests.
    1. _____
    2. _____

2. What distinguishes clinical genetic tests from direct-to-consumer genetic tests?

3. According to the Genetic Information Nondiscrimination Act (GINA), which scenario is true?
    a. Your clinical genetic test results are private, even your doctor is not allowed to view the results without your consent.
    b. Your clinical genetic test results are public, because genetic information should be accessible to everyone.
    c. Your genetic test results will be used by your health insurance company to find specific medical procedures and treatments based on your unique genetic code.
    d. Your genetic test results cannot be used by your employer to make decisions about your employment status.

Activity

Sam and their family have different views on DNA ancestry tests. Why do some people feel excited about ancestry tests while others feel hesitant? Use this activity to explore different ancestry testing companies, learn the information these tests can reveal and what features they offer. At the end of the activity, consider stories from people who took these tests and explore jobs that relate to the themes discussed throughout this lesson.

Part 1. Research different ancestry testing companies

There are many companies that offer ancestry testing, each with their own approach and features. Use the internet to find two ancestry testing companies to research thoroughly. You can select any two companies that analyze human ancestry, but if you need some options, you could select *23andMe* or *AncestryDNA*. As you perform your research, use **Table 1 Ancestry Testing Companies** to record key information about each company and what they offer.

Table 1. Ancestry Testing Companies

Company name		
Website		
Types of tests offered (like autosomal DNA or Y-chromosome DNA)		
Geographic regions covered in ancestry analysis		
Depth of ancestry analysis provided (like migration patterns or breakdown of ethnicities)		
Additional features or services (like family matching or health insights)		
Privacy policies or considerations for genetic data sharing		
Other interesting features		

Now that you've completed your research into both ancestry testing companies, compare the information about the two companies and observe the similarities and differences between them. Answer the following questions.

1. What are the most notable differences between the two companies?

2. Did one company offer a broader range of tests or more specialized analysis?

3. Consider the geographic regions covered in ancestry analysis in each company. Did you notice any differences between the two companies in terms of depth or specificity of regional data provided?

4. Consider the additional features and services from each company. Did one company offer unique insights or tools that stood out to you?

5. How did each company discuss genetic data privacy? Was this information easy to find?

6. Do you have any lingering questions or areas for further exploration that arose from your research and comparison?

7. How might the information you gathered influence your decision to choose a testing service for yourself or your family?

Part 2. Ethics

Ancestry testing can reveal fascinating insights into a person's genetic heritage, providing a glimpse into the unknown histories of a person's origins. However, along with these discoveries come important ethical questions about the potential impact of unexpected information on individuals and families.

First, hear from real people about their experiences with ancestry tests. Choose one of the resources below and read, listen, or watch what is presented. Answer the following questions about the resource you chose.

- ARTICLE from BBC News: These people took DNA tests. The results changed their lives. *<https://www.bbc.com/future/article/20231004-these-people-took-dna-tests-the-results-changed-their-lives>*
- PODCAST from In Those Genes: Up In Dem' Genes *<https://player.audiostaq.com/inthosegenes/up_in_dem_genes>*
- VIDEO from The National Human Genome Research Institute: The Human Genome: Who Do We Think We Are? *<https://www.youtube.com/watch?v=lltW_13Nvps>*

1. What was the primary message of the resource you explored?

2. What surprised you most about the information discussed?

Next, explore hypothetical scenarios to delve into the complex ethical dilemmas that can arise from ancestry testing results. Consider the emotional, psychological, and social implications of unexpected findings and the ethical responsibilities of both individuals and ancestry testing companies.

Choose one scenario from the list below and carefully read and analyze it. Be sure to consider the emotions, dilemmas, and ethical considerations faced by the individual(s) involved. Answer the following questions.

- **Scenario 1:** Boshen's ancestry test results reveal he has a different biological father than the one he grew up with. He must decide whether to confront his family and seek out his biological father. This discovery leaves him grappling with questions about his identity and family relationships.
- **Scenario 2:** Siblings Kia and Kristin find out through ancestry tests that they have different ethnic backgrounds, raising questions about their family history. They wonder whether their parents have been keeping secrets or if something unexpected explains their results. This leads them to reconsider their understanding of their heritage and their bond as sisters.
- **Scenario 3:** Adina learns through an ancestry test that she has a previously unknown half-sibling who reaches out to connect. Adina must decide whether to meet this sibling and what this new relationship might mean for her family. She is unsure how this will affect her sense of belonging.
- **Scenario 4:** Rolando's ancestry test reveals a predisposition to a hereditary health condition, causing him anxiety about his future. He now must decide whether to seek further medical advice or simply monitor his health. Rolando also wonders if he should share this information with his family, as it could affect them too.

3. How might the individual(s) in the case study feel upon receiving unexpected information from their ancestry test results?

4. What are the potential emotional, psychological, and social implications of discovering such information?

5. How might unexpected information impact family dynamics and relationships?

6. What ethical considerations should be considered when sharing or acting on unexpected ancestry test results?

Finally, reflect on the work you just completed and think about yourself, your family, and your own feelings. Answer the following questions.

7. How do you think you would react if you received unexpected information from an ancestry test?

8. What responsibilities do ancestry testing companies have in disclosing potentially sensitive or surprising information to their customers?

9. Should individuals have the right to choose whether to receive certain types of genetic information from ancestry tests?

10. What role does informed consent play in ancestry testing, particularly regarding potential surprises or unexpected findings?

Part 3. Careers

Explore jobs and career paths that relate to this activity.

1. Navigate to any job search site. Some recommended ones are
   - Indeed: https://www.indeed.com/salaries
   - Zippa: https://www.zippia.com/careers
   - JobViz: https://www.galacticpolymath.com/jobviz

2. Search for the jobs from this activity. You can also find more jobs using keywords from the activity or explore jobs and categories on the site.

   Genetic Counselors advise people before and after genetic tests. Similar jobs include Genetic Counseling Assistant and Research Genetic Counselor.

   Computational Biologists use data, modeling, and computers to understand biological phenomena. Similar jobs include Computer Scientist and Bioinformatician.

   Data Privacy Officers work on issues of cyber security like protecting data. Similar jobs include Information Security Analyst and Cyber Security Specialist.

3. Fill in the table below with 2 jobs that interest you. Record the job title, degree(s) and training needed, and the salary estimate. You can also write a description of the work and any other notes about why you found the job interesting. Continue filling the table with more jobs if you want to.

Job title	Degree(s)/training needed	Salary estimate	Description of work	Notes

4. Hear from people in some of the jobs you just discovered. Choose 1 resource, then use the table below to record the resource you explored, as well as your thoughts about the people and the jobs they do. Continue filling the table with more jobs if you want to.
    - JAX Career Chats: Genetic Counselor
    - I Am A Scientist: Computational Biologist
    - LabXChange Narrative: Cyber Security Specialist

Resource you explored	Person name and job title	In your own words, describe the work they do	Which of their traits match your skills and interests?	What do you want to learn more about?

Glossary

Ancestry tests – a type of direct-to-consumer genetic test that examines common DNA variations in groups of individuals to find similarities and predict their most likely global ethnic origins.

Chromosome – A structure that contains DNA, the genetic information of an organism.

Clinical genetic tests – A category of genetic tests that are done through healthcare providers like doctors.

Deoxyribonucleic acid (DNA) – A biological molecule of which the primary role is the storage of genetic information. DNA is made of deoxyribonucleotides. The nitrogenous bases found in DNA include adenine (A), guanine (G), cytosine (C), and thymine (T).

Direct-to-consumer genetic tests – A category of genetic tests that are purchased by customers.

Genetic tests – A broad category of laboratory test that looks for changes in DNA, RNA, or proteins.

Genome – The complete set of chromosomes, or genetic material, of an organism or cell.

Karyotype – The complete set of chromosomes in the cells of an individual.

Pedigree – also known as a family tree, a diagram showing the relationship between family members. Pedigrees can be used to show how genetic traits or conditions are inherited across generations.

Protein – A biological molecule composed of amino acids. Proteins are essential for life and have many important functions in the body.

Ribonucleic acid (RNA) – A biological molecule that contains genetic information. RNA is made of ribonucleotides and can take different forms, such as messenger RNA (mRNA), transfer RNA (tRNA), and microRNA (miRNA). The nitrogenous bases found in RNA are adenine (A), guanine (G), cytosine (C), and uracil (U).

Tumor – An abnormal growth of tissue that can be either benign or malignant (cancerous).

Activity 2: Sequence Comparison in Ancestry Testing – Paper-based Activity

Sam's Story: How does ancestry testing work?

Sam is a high school student who wants a DNA ancestry test for their 18th birthday. At school, Sam approaches their biology teacher Dr. V to share their excitement about taking this at-home genetic test. But Sam is surprised to learn the test doesn't work the way they thought it would.

Read the scene below from Sam's life. If you're in a class or group, assign one person as Sam, and one person as Dr. V, and read the scene out loud.

> **Sam:** *Dr. V! I asked for a DNA ancestry test for my 18th birthday! I am so excited to get all of my DNA sequenced!*
>
> **Dr. V:** *That's not exactly how these tests work, Sam. Only a portion of our genomes are examined in ancestry tests.*
>
> **Sam:** *What?! What are just a few DNA sites going to tell you?!*
>
> **Dr. V:** *Let's do an exercise together to learn how these tests really work.*

Prediction

From their discussion in class, Sam might not fully understand how ancestry tests work. How do you think an ancestry test works? Create a flowchart outlining the steps involved in an ancestry test. Think about sample collection, what information is analyzed by the company, and what results are shared.

Background

Dr. V wants to teach the class how ancestry tests work. Before getting into the details of the test, first she prepares the class with some important background information. Dr. V will review concepts from Biology class on genetics and inheritance, and also explore new topics on alleles and sequencing.

Bolded words are defined in the Glossary at the end of this lesson.

Genetics & Inheritance

DNA is a biological molecule comprised of a four-letter code of the **nucleotides** adenine (A), thymine (T), cytosine (C) and guanine (G). The human **genome** is the complete set of DNA in an individual that encodes the instructions for making each of us who we are.

Human genomes are 99.9% identical between individuals. Only 0.1% of our DNA is different between individuals! Variation in this 0.1% of DNA are the **genotypic** differences that leads to the **phenotypic** differences we see around us. When only one DNA nucleotide varies, this is called a **single nucleotide polymorphism (SNP)** or **single nucleotide variant (SNV)**.

Humans have **diploid** genomes, which means they have two copies of every piece of DNA. One copy is passed from each **gamete:** one copy from the **haploid** sperm cell, and one copy is passed from the haploid egg cell. Thus, an individual inherits two copies, one from each biological parent, for any given genomic location.

Let's look at an example in Figure 1. Here, the blue DNA on the left represents the sperm haploid genome, and the yellow DNA on the right represents the egg haploid genome. These cells come together to make an offspring, shown here as an individual with a diploid genome inherited from both the sperm and the egg.

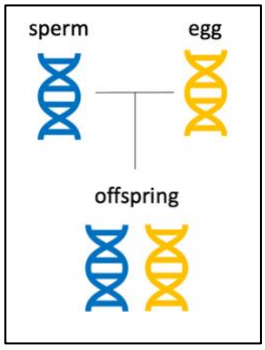


Figure 1. Haploid sperm and eggs cells come together to make a diploid offspring.

At any location in the genome, the genotype of the offspring will depend on the DNA they inherited from both biological parents. An individual inherits two copies of DNA, one from the sperm and one from the egg. Each copy, or version of DNA, is called an **allele**. At any DNA **locus**, if the two inherited alleles are the same, the individual is **homozygous** at that locus. If the alleles are different, the individual is **heterozygous**.

Let's examine one specific DNA locus in the genome that is known to contain a SNP in Figure 2. Here at the circled locus, we observe the sperm cell carries a G allele, and the egg cell carries an A allele. Since the offspring inherits one allele from each parent, the offspring's genotype is heterozygous at this locus.

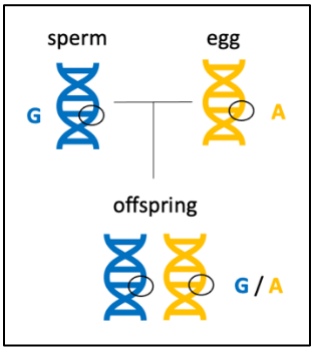


Figure 2. An offspring's genotype at one locus is determined by what alleles they inherit.

Each site of our genomes can be examined in the same way to observe which individuals carry which DNA variants. Looking at another SNP at a different DNA locus in Figure 3, we observe that here the sperm cell carries an A allele, and the egg cell carries a T allele, resulting in an offspring that is heterozygous at this locus.

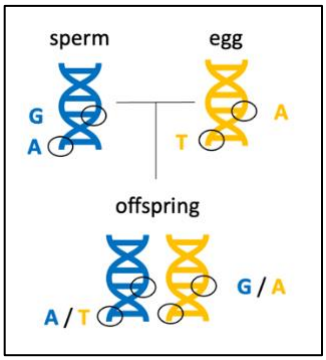


Figure 3. Different regions of the genome can carry different alleles, or variants, across individuals.

Allele Frequencies

Counting alleles in individuals reveals **allele frequencies**. This is a measure of the distribution of all DNA variations (alleles) in a **population**. It can be calculated very simply once you know the number of each allele observed in your population, as well as the total number of individuals in your population. The formula is:

$$Allele\ Frequency = \frac{v}{2N}$$

Where the **variable** v is the number of each variant allele detected in the dataset, and the variable N is the total number of diploid individuals in the dataset. Written another way without variables, the formula for allele frequency is:

$$Allele\ Frequency = \frac{Allele\ count\ of\ a\ specific\ allele\ in\ the\ population}{Total\ allele\ count\ in\ the\ population}$$

This allele frequency number can either be reported as a fraction or as a percent. To report as a fraction, the calculation ends with the formulas as shown above. To report as a percent, the number is multiplied by 100:

$$Allele\ Frequency\ (percent) = \frac{v}{2N} * 100$$

$$Allele\ Frequency\ (percent) = \frac{Allele\ count\ of\ a\ specific\ allele\ in\ the\ population}{Total\ allele\ count\ in\ the\ population} * 100$$

Let's work through an example of this by returning to our example. In Figure 4, the genomes of the two parents of the offspring are now revealed, and the genotypes at the first DNA site are shown for all three individuals.

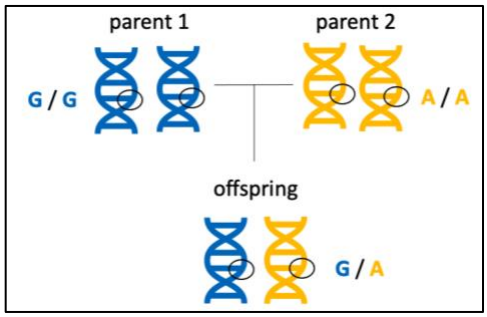


Figure 4. The genomes of the parents are revealed and the genotypes of all 3 individuals are known at this DNA site.

We can count how many of each variant allele we detect in this dataset and calculate allele frequencies for each allele at DNA site 1. Recall that at every DNA locus, there are four possible variant alleles for the four DNA nucleotides: either an A, T, C, or G will be present. In this example, there are 3 individuals total which is the population of this dataset. There are no C or T alleles. A total of 3 G alleles and 3 A alleles are present. This can be recorded in a table, like in Figure 5.

	Allele count at DNA SNP site 1
C	0
T	0
A	3
G	3

Dataset: N = 3 individuals

Figure 5. Each variant allele from Figure 5 at DNA SNP site 1 is counted and entered into the table.

Now the allele frequency fraction for each variant allele can be calculated as follows:

$$C\ Allele\ Frequency\ at\ SNP\ 1 = \frac{Allele\ count\ of\ C\ allele\ in\ the\ population}{Total\ allele\ count\ in\ the\ population} = \frac{0}{6} = 0$$

$$T\ Allele\ Frequency\ at\ SNP\ 1 = \frac{Allele\ count\ of\ T\ allele\ in\ the\ population}{Total\ allele\ count\ in\ the\ population} = \frac{0}{6} = 0$$

$$A\ Allele\ Frequency\ at\ SNP\ 1 = \frac{Allele\ count\ of\ A\ allele\ in\ the\ population}{Total\ allele\ count\ in\ the\ population} = \frac{3}{6} = 0.5$$

$$G\ Allele\ Frequency\ at\ SNP\ 1 = \frac{Allele\ count\ of\ G\ allele\ in\ the\ population}{Total\ allele\ count\ in\ the\ population} = \frac{3}{6} = 0.5$$

Remember that these allele frequencies can also be reported as percentages. The allele frequency percent for each variant allele would be:

$$C\ Allele\ Frequency\ at\ SNP\ 1 = \ 0 * 100 = 0\ \%$$

$$T\ Allele\ Frequency\ at\ SNP\ 1 = \ 0 * 100 = 0\ \%$$

$$A\ Allele\ Frequency\ at\ SNP\ 1 = \ 0.5 * 100 = 50\ \%$$

$$G\ Allele\ Frequency\ at\ SNP\ 1 = \ 0.5 * 100 = 50\ \%$$

Recall that allele frequencies represent the proportion of each DNA variant allele observed in the population. But, what is that population? In our example, we know our dataset is only 3 individuals, and they are biologically related which means they share DNA. Allele frequency data can change based on the population dataset size and the diversity of individuals.

For example, let's examine the same DNA SNP site 1 in two datasets with a different number of individuals in Figure 6. Our example with 3 individuals gives very different allele frequency numbers than looking at 50 individuals in a larger, more diverse dataset. Graphing this data as a pie chart gives us another representation of the same data, which shows clearly the drastic different in frequencies of each allele with a bigger and more diverse dataset.

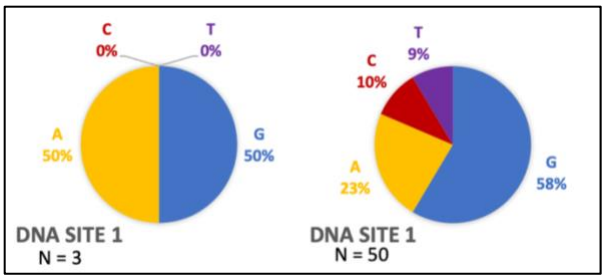


Figure 6. The allele frequencies at any DNA site can change based on the population examined.

DNA Sequencing

Ancestry testing companies typically perform this type of SNP genotyping at DNA sites with known and high variation. Interestingly, some medical tests also use similar technology to detect known variants. Whole genome sequencing is not typically performed in ancestry tests.

Spreadsheets and Tables

Spreadsheets and tables are used to display information from different analyses. Each unit of a spreadsheet or table is a **cell**, and information such as numbers, dates, or words can be entered. When information from multiple cells is arranged **vertically**, it forms a **column**. When information from multiple cells is arranged **horizontally**, it forms a **row**. **Headers** are cells with descriptions that provide additional information about what is in a row or in a column.

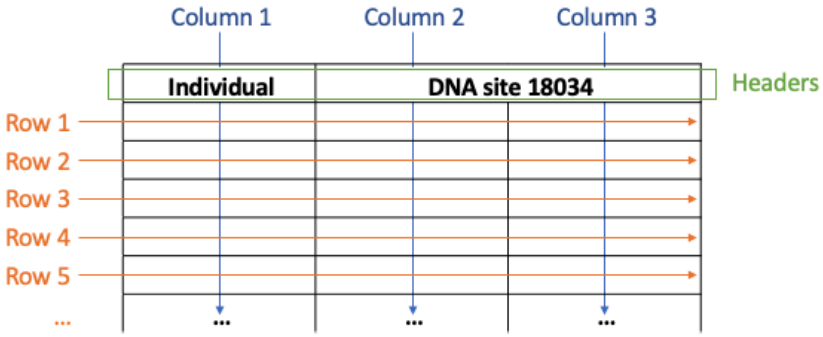


Figure 7. A table or spreadsheet has many cells of information. Columns, rows, and headers are highlighted.

We already saw an example of a table in Table 1. Each DNA nucleotide is a row with one piece of information that corresponds to it: an allele count number. The allele count number is a column, and has a descriptive header. Go back to review that table to notice the features: it has 2 columns of information, one with a header, and there are 4 rows of data.

Quick Knowledge Check

Check your understanding of the background material by answering these questions.

1. What statement best describes alleles?
    a. Haploid gamete cells with a single set of chromosomes.
    b. Two alternative forms of a gene that arose from DNA variations.
    c. Diploid genomes with two sets of chromosomes.
    d. Individuals with various genotypes in a population.

2. True or false? Allele frequency calculations must be calculated for each allele separately.

3. Draw a table with 2 columns and 3 rows. How many cells total are in this table?

Activity

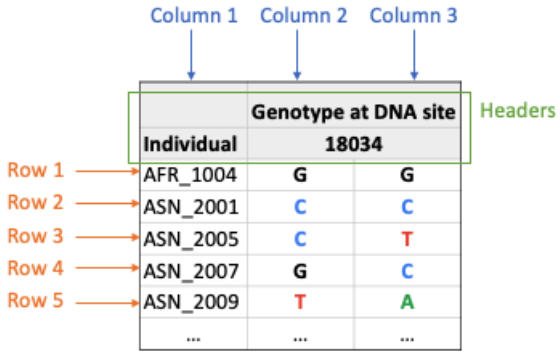
Dr. V shows Sam and the rest of the class an example of an ancestry testing company called *23Chromosomes* that is building a reference DNA database. *23Chromosomes* selected 50 individuals who volunteered to share their genetic information with the company. These carefully selected individuals represent 5 populations from around the world: African, Asian, European, Native American, and Pacific Islander. *23Chromosomes* will use the genetic data from these individuals to build their own DNA **reference database**.

Follow along with Dr. V's example to analyze the data from *23Chromosomes* and learn how DNA ancestry tests work. Calculate the allele frequencies for different alleles across populations and identify which alleles are associated with which populations.

Part 1. Explore the data

The genomic technologies division of *23Chromosomes* performed SNP genotyping on 50 individuals from 5 regions around the world. They delivered the genotype data in spreadsheets and sent it to the computational biology team for analysis.

First, let's observe part of the data in the spreadsheets you chose to learn how it is organized. This image shows part of Table 1 for DNA Site 18034, with the rows, columns, and headers identified. Use this table shown to answer the questions that follow.



a. Record the name of the Column 1 header.

b. How many individuals are displayed in the portion of the table shown?

c. The individuals are distinguished from one another by a 3-letter code, an underscore, and a 4-number code. Based on what you know about the origin of this data, what do the 3 letters represent?

d. Which geographic regions are represented in the individuals shown in this part of the table?

e. Record the name of the header for Columns 2 and 3.

f. Why are there two columns for this header?

g. Record the genotype for the individual in Column 1, Row 1.

h. Choose another individual and record their information:
Population:
Individual number:
Genotype at DNA site 18034:

Part 2. Organize the data

Now that we're more familiar with the data, it's time to start working with the data from *23Chromosomes*.

Find all data from *23Chromosomes* at the end of this handout. There are five spreadsheets, each with genotype data from one of the five DNA sites (SNPs) in all 50 individuals. Choose one of the five DNA sites to start and focus on **Table 1 Genotype Data**.

Table 1 contains the genotype data from 50 individuals in all five populations at one DNA site. This data is already organized: the data is sorted by population.

Part 3. Count alleles

The genotype data in Table 1 is organized with all individuals grouped by population. Now, the alleles for all individuals can be counted more easily.

Find **Table 2 Allele Count Data** for the DNA site you are working on. Next, use the sorted Table 1 to count each allele, for the given DNA site, in each population. Record your results in Table 2. Continue counting each variant for all 10 individuals in the population. Repeat this for all five regions. Total your counts and enter them into the appropriate cells in Table 2.

Part 4. Calculate allele frequency

Now that you calculated how many variants are detected in the individuals at each DNA site, you can calculate the allele frequency, or the proportion of each variant, in each population.

Find **Table 3 Allele Frequency Percent Data** for the DNA site you are working on. Use the allele count data you previously generated in Table 2 to calculate the allele frequency percent in each population.

Recall that the formula to calculate allele frequency percent is:

$$Allele\ Frequency = \frac{Allele\ count\ of\ a\ specific\ allele\ in\ the\ population}{Total\ allele\ count\ in\ the\ population} * 100$$

Continue your calculations for each variant for all 10 individuals in each population. Repeat this for all five regions. Record your results in the appropriate cells in Table 3.

Part 5. Compare allele frequency data

Look at the allele frequency data from all five DNA sites in all five populations. First, compare the numbers for the allele frequencies at one DNA site across all populations. Then, compare the numbers for allele frequencies in one population across all DNA sites. What do you notice? Choose at least three of the following questions and record your answers below.

1. What biological concepts can explain these observations?

2. Why don't all individuals from the same population have the same genotypes?

3. Why do some populations have the same frequencies at some DNA sites?

4. Would you expect a different ancestry testing company to have the same allele frequency data for these populations?

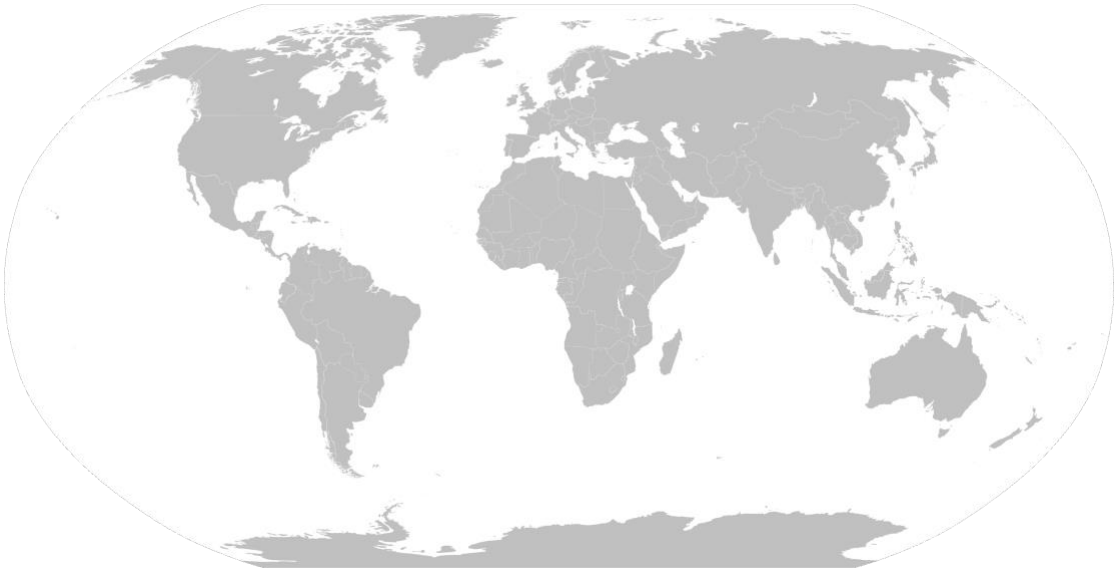
5. What would the data look like if we had 500 individuals? What about 500,000 individuals?

6. What would make you more confident in the data?

Part 6. Ethics

The company *23Chromosomes* used data from individuals from 5 populations: African (AFR), Asian (ASN), European (EUR), Native American (NAM), and Pacific Islander (PIS).

Using the map provided, circle and label the areas that correspond to each region. If you're in a group or class, work independently, then compare your answers with your peers when everyone has finished. Then choose at least three of the following questions and record your answers below.



1. If you compared with your peers, did you have different answers? Which version is correct?

2. What areas of the world are not covered?

3. What about countries that span more than one continent?

4. How did you define Asian? Native American? European?

5. How large is each region?

6. How many modern-day countries are in each region?

7. How would you have defined these regions 100 years ago? How might these regions change 100 years from now?

Part 7. Careers

Explore jobs and career paths that relate to this activity.

1. Navigate to any job search site. Some recommended ones are
   - Indeed: https://www.indeed.com/salaries
   - Zippa: https://www.zippia.com/careers
   - JobViz: https://www.galacticpolymath.com/jobviz

2. Search for the jobs from this activity. You can also find more jobs using keywords from the activity or explore jobs and categories on the site.

   Bioinformaticians analyze genomic data. Similar jobs include Data Scientist and Bioinformatics Analyst.

   Genomic Technologists perform DNA sequencing assays. Similar jobs include Laboratory Technician and Research Technician.

   Population Geneticists study the genetics of groups of individuals, like humans. Similar jobs include Computational Geneticist and Statistical Geneticist.

3. Fill in the table below with 2 jobs that interest you. Record the job title, degree(s) and training needed, and the salary estimate. You can also write a description of the work and any other notes about why you found the job interesting. Continue filling the table with more jobs if you want to.

Job title	Degree(s)/training needed	Salary estimate	Description of work	Notes

4. Hear from people in some of the jobs you just discovered. Choose 1 resource, then use the table below to record the resource you explored, as well as your thoughts about the people and the jobs they do. Continue filling the table with more jobs if you want to.
    - JAX Career Chats: Bioinformatics Analyst
    - JAX Career Spotlight: Genomic Technologist
    - I Am A Scientist: Population Geneticist

Resource you explored	Person name and job title	In your own words, describe the work they do	Which of their traits match your skills and interests?	What do you want to learn more about?

Glossary

Allele – One of several alternative forms of a gene. Alleles for a given gene have different DNA sequences, which can lead to different phenotypes. In a diploid cell, each cell has two alleles for each gene (one from each parent). These two alleles will be found at the same position (locus) on homologous chromosomes.

Allele frequency – The fraction of all chromosomes in a population that carry a specific allele over the total population.

Cell – In a spreadsheet or table, a cell is one unit where information such as numbers or words can be entered.

Column – In a spreadsheet, when information from multiple cells is arranged vertically.

Deoxyribonucleic acid (DNA) – A biological molecule of which the primary role is the storage of genetic information. DNA is made of deoxyribonucleotides. The nitrogenous bases found in DNA include adenine (A), guanine (G), cytosine (C) and thymine (T).

Gamete – A gamete is a reproductive cell of an animal or plant, such as egg and sperm cells. In animals, these cells are haploid and carry only one copy of each chromosome.

Genome – The complete set of chromosomes, or genetic material, of an organism or cell.

Genotype – The genetic makeup of an organism (whereas the term phenotype describes the physical traits of an organism). The term genotype can be used to describe which alleles an individual has for a single gene. When describing one particular gene, genotype refers to the pair of alleles inherited by the organism for that gene. The term genotype can also be used to describe the complete set of a cell's or an organism's genes. For example, humans have about 20,000 genes, so a genotype would indicate which alleles are present for each of those genes.

Header – In a spreadsheet, cells that have descriptions that provide additional information about what is in a row or column.

Homozygous – Having two identical alleles for a given gene (ie, the same allele was inherited from each parent).

Horizontal – A direction that is parallel to the plan of the horizon, at right angles to the vertical.

Locus – A locus in genomics is a physical location within the genome. It can be a region like a gene or portion of a gene, or a specific nucleotide or set of nucleotides.

Nucleotide – The building blocks of nucleic acids (DNA and RNA) comprised of a nitrogenous base, five-carbon sugar, and phosphate.

Phenotype – The observable characteristics of a cell or organism.

Population – In biology, a population is the total number of individuals in a specific area.

Reference genome – A template genome for organism. This genetic resource is a digital nucleic acid sequence database, assembled by scientists as a representative example of the genomic features in one idealized individual.

Row – In a spreadsheet, when information from multiple cells is arranged horizontally.

Sequencing – Sequencing is a technique that is used in molecular biology to determine the order of nucleotides in a particular DNA or RNA molecule. It involves identifying the specific order of nucleotides that make up the molecule, which can provide important information about the genetic code of an organism. Sequencing can be done using a variety of methods, including Sanger sequencing, next-generation sequencing, and single-molecule sequencing.

Single nucleotide polymorphism – A single nucleotide polymorphism (abbreviated as SNP, pronounced as *snip*) is a type of genomic variant when one single nucleotide in the DNA is changed. Also known as a single nucleotide variant (abbreviated as SNV).

Variable – In mathematics, a variable is a symbol (such as v, N, or x) that represents an object (such as a number).

Variant – A change or difference in the DNA sequence of a cell or organism.

Vertical – A direction where the top is directly above the bottom, at right angles to the horizontal.

23Chromosomes data: DNA Site 18034

[DNA site 18034] Table 1. Genotype data

	Genotype at DNA site	
Individual	**18034**	
AFR_1001	G	G
AFR_1002	T	C
AFR_1003	G	G
AFR_1004	G	G
AFR_1005	G	G
AFR_1006	C	C
AFR_1007	T	A
AFR_1008	T	G
AFR_1009	G	G
AFR_1010	G	G
ASN_2001	C	C
ASN_2002	T	G
ASN_2003	A	T
ASN_2004	T	A
ASN_2005	C	T
ASN_2006	C	C
ASN_2007	G	C
ASN_2008	A	T
ASN_2009	T	A
ASN_2010	T	T
EUR_3001	T	G
EUR_3002	A	G
EUR_3003	G	C
EUR_3004	C	G
EUR_3005	C	G
EUR_3006	G	G
EUR_3007	C	G
EUR_3008	C	G
EUR_3009	C	C
EUR_3010	C	C
NAM_4001	C	A
NAM_4002	T	A
NAM_4003	G	A
NAM_4004	A	T
NAM_4005	T	A
NAM_4006	A	A
NAM_4007	A	C
NAM_4008	A	A
NAM_4009	A	A
NAM_4010	A	T
PIS_5001	G	T
PIS_5002	T	C
PIS_5003	C	C
PIS_5004	C	T
PIS_5005	C	A
PIS_5006	T	G
PIS_5007	C	C
PIS_5008	C	C
PIS_5009	C	T
PIS_5010	T	G

[DNA site 18034] Table 2. Allele count data

	Allele count at DNA site 18034				
	African	Asian	European	Native American	Pacific Islander
C allele					
T allele					
A allele					
G allele					
Total allele count					

[DNA site 18034] Table 3. Allele frequency percent data

	Allele frequency percent at DNA site 18034				
	African	Asian	European	Native American	Pacific Islander
C allele					
T allele					
A allele					
G allele					
Total allele count					

23Chromosomes data: DNA Site 46754

[DNA site 46754] Table 1. Genotype data

	Genotype at DNA site	
Individual	**46754**	
AFR_1001	C	A
AFR_1002	A	T
AFR_1003	A	A
AFR_1004	G	G
AFR_1005	A	A
AFR_1006	A	A
AFR_1007	G	A
AFR_1008	T	G
AFR_1009	C	A
AFR_1010	T	C
ASN_2001	G	C
ASN_2002	C	C
ASN_2003	A	C
ASN_2004	C	T
ASN_2005	G	T
ASN_2006	G	C
ASN_2007	C	C
ASN_2008	G	A
ASN_2009	A	C
ASN_2010	A	C
EUR_3001	A	C
EUR_3002	A	C
EUR_3003	A	A
EUR_3004	A	A
EUR_3005	A	A
EUR_3006	G	A
EUR_3007	A	T
EUR_3008	A	A
EUR_3009	A	A
EUR_3010	G	A
NAM_4001	C	G
NAM_4002	T	C
NAM_4003	C	C
NAM_4004	A	T
NAM_4005	C	C
NAM_4006	T	C
NAM_4007	C	C
NAM_4008	C	G
NAM_4009	C	A
NAM_4010	T	C
PIS_5001	C	T
PIS_5002	T	A
PIS_5003	G	C
PIS_5004	G	C
PIS_5005	A	A
PIS_5006	C	C
PIS_5007	C	C
PIS_5008	A	A
PIS_5009	T	G
PIS_5010	G	C

[DNA site 46754] Table 2. Allele count data

	Allele count at DNA site 46754				
	African	Asian	European	Native American	Pacific Islander
C allele					
T allele					
A allele					
G allele					
Total allele count					

[DNA site 46754] Table 3. Allele frequency percent data

	Allele frequency percent at DNA site 46754				
	African	Asian	European	Native American	Pacific Islander
C allele					
T allele					
A allele					
G allele					
Total allele count					

23Chromosomes data: DNA Site 53134

[DNA site 53134] Table 1. Genotype data

	Genotype at DNA site	
Individual	**53134**	
AFR_1001	T	A
AFR_1002	G	C
AFR_1003	G	T
AFR_1004	G	G
AFR_1005	C	C
AFR_1006	G	G
AFR_1007	T	T
AFR_1008	A	A
AFR_1009	C	G
AFR_1010	G	C
ASN_2001	C	C
ASN_2002	C	G
ASN_2003	A	T
ASN_2004	T	T
ASN_2005	C	C
ASN_2006	A	C
ASN_2007	T	G
ASN_2008	T	A
ASN_2009	C	T
ASN_2010	G	C
EUR_3001	G	G
EUR_3002	G	G
EUR_3003	G	G
EUR_3004	A	C
EUR_3005	G	G
EUR_3006	C	A
EUR_3007	G	G
EUR_3008	G	G
EUR_3009	G	G
EUR_3010	G	G
NAM_4001	C	G
NAM_4002	G	C
NAM_4003	G	G
NAM_4004	G	G
NAM_4005	G	C
NAM_4006	G	C
NAM_4007	T	T
NAM_4008	C	G
NAM_4009	C	G
NAM_4010	A	G
PIS_5001	C	C
PIS_5002	G	T
PIS_5003	T	T
PIS_5004	T	T
PIS_5005	A	T
PIS_5006	T	T
PIS_5007	T	T
PIS_5008	T	G
PIS_5009	C	C
PIS_5010	A	T

[DNA site 53134] Table 2. Allele count data

	Allele count at DNA site 53134				
	African	Asian	European	Native American	Pacific Islander
C allele					
T allele					
A allele					
G allele					
Total allele count					

[DNA site 53134] Table 3. Allele frequency percent data

	Allele frequency percent at DNA site 53134				
	African	Asian	European	Native American	Pacific Islander
C allele					
T allele					
A allele					
G allele					
Total allele count					

23Chromosomes data: DNA Site 95005

[DNA site 95005] Table 1. Genotype data

	Genotype at DNA site	
Individual	**95005**	
AFR_1001	C	A
AFR_1002	G	C
AFR_1003	A	T
AFR_1004	T	T
AFR_1005	C	C
AFR_1006	C	C
AFR_1007	T	C
AFR_1008	T	A
AFR_1009	G	C
AFR_1010	C	T
ASN_2001	C	C
ASN_2002	T	A
ASN_2003	A	G
ASN_2004	G	G
ASN_2005	G	T
ASN_2006	G	A
ASN_2007	G	G
ASN_2008	A	A
ASN_2009	A	G
ASN_2010	T	A
EUR_3001	C	T
EUR_3002	G	T
EUR_3003	G	G
EUR_3004	G	C
EUR_3005	G	T
EUR_3006	G	C
EUR_3007	T	G
EUR_3008	G	G
EUR_3009	A	A
EUR_3010	A	C
NAM_4001	T	G
NAM_4002	C	G
NAM_4003	C	C
NAM_4004	C	C
NAM_4005	A	A
NAM_4006	G	C
NAM_4007	C	C
NAM_4008	C	C
NAM_4009	C	C
NAM_4010	G	C
PIS_5001	A	A
PIS_5002	A	A
PIS_5003	A	A
PIS_5004	A	T
PIS_5005	A	G
PIS_5006	A	T
PIS_5007	A	A
PIS_5008	A	A
PIS_5009	A	A
PIS_5010	T	A

[DNA site 95005] Table 2. Allele count data

	Allele count at DNA site 95005				
	African	Asian	European	Native American	Pacific Islander
C allele					
T allele					
A allele					
G allele					
Total allele count					

[DNA site 95005] Table 3. Allele frequency percent data

	Allele frequency percent at DNA site 95005				
	African	Asian	European	Native American	Pacific Islander
C allele					
T allele					
A allele					
G allele					
Total allele count					

23Chromosomes data: DNA Site 123030

[DNA site 123030] Table 1. Genotype data

	Genotype at DNA site	
Individual	**123030**	
AFR_1001	T	T
AFR_1002	A	A
AFR_1003	A	C
AFR_1004	G	T
AFR_1005	T	T
AFR_1006	T	T
AFR_1007	T	T
AFR_1008	C	C
AFR_1009	T	T
AFR_1010	T	A
ASN_2001	C	C
ASN_2002	A	G
ASN_2003	A	A
ASN_2004	G	C
ASN_2005	A	A
ASN_2006	C	A
ASN_2007	G	A
ASN_2008	G	A
ASN_2009	A	C
ASN_2010	C	T
EUR_3001	G	T
EUR_3002	G	A
EUR_3003	G	G
EUR_3004	T	G
EUR_3005	G	G
EUR_3006	G	A
EUR_3007	C	G
EUR_3008	G	G
EUR_3009	A	G
EUR_3010	G	G
NAM_4001	C	T
NAM_4002	A	C
NAM_4003	A	A
NAM_4004	C	C
NAM_4005	T	G
NAM_4006	C	G
NAM_4007	C	G
NAM_4008	A	A
NAM_4009	G	G
NAM_4010	C	C
PIS_5001	T	G
PIS_5002	T	T
PIS_5003	C	C
PIS_5004	T	T
PIS_5005	C	C
PIS_5006	T	T
PIS_5007	C	C
PIS_5008	T	G
PIS_5009	C	C
PIS_5010	C	C

[DNA site 12303] Table 2. Allele count data

	Allele count at DNA site 12303				
	African	Asian	European	Native American	Pacific Islander
C allele					
T allele					
A allele					
G allele					
Total allele count					

[DNA site 12303] Table 3. Allele frequency percent data

	Allele frequency percent at DNA site 12303				
	African	Asian	European	Native American	Pacific Islander
C allele					
T allele					
A allele					
G allele					
Total allele count					

Activity 2: Sequence Comparison in Ancestry Testing – Spreadsheet-based Activity

Sam's Story: How does ancestry testing work?

Sam is a high school student who wants a DNA ancestry test for their 18th birthday. At school, Sam approaches their biology teacher Dr. V to share their excitement about taking this at-home genetic test. But Sam is surprised to learn the test doesn't work the way they thought it would.

Read the scene below from Sam's life. If you're in a class or group, assign one person as Sam, and one person as Dr. V, and read the scene out loud.

> **Sam:** *Dr. V! I asked for a DNA ancestry test for my 18th birthday! I am so excited to get all of my DNA sequenced!*
>
> **Dr. V:** *That's not exactly how these tests work, Sam. Only a portion of our genomes are examined in ancestry tests.*
>
> **Sam:** *What?! What are just a few DNA sites going to tell you?!*
>
> **Dr. V:** *Let's do an exercise together to learn how these tests really work.*

Prediction

From their discussion in class, Sam might not fully understand how ancestry tests work. How do you think an ancestry test works? Create a flowchart outlining the steps involved in an ancestry test. Think about sample collection, what information is analyzed by the company, and what results are shared.

Background

Dr. V wants to teach the class how ancestry tests work. Before getting into the details of the test, first she prepares the class with some important background information. Dr. V will review concepts from Biology class on genetics and inheritance, and also explore new topics on alleles and sequencing.

Bolded words are defined in the Glossary at the end of this lesson.

Genetics & Inheritance

DNA is a biological molecule comprised of a four-letter code of the **nucleotides** adenine (A), thymine (T), cytosine (C) and guanine (G). The human **genome** is the complete set of DNA in an individual that encodes the instructions for making each of us who we are.

Human genomes are 99.9% identical between individuals. Only 0.1% of our DNA is different between individuals! Variation in this 0.1% of DNA are the **genotypic** differences that leads to the **phenotypic** differences we see around us. When only one DNA nucleotide varies, this is called a **single nucleotide polymorphism (SNP)** or **single nucleotide variant (SNV)**.

Humans have **diploid** genomes, which means they have two copies of every piece of DNA. One copy is passed from each **gamete:** one copy from the **haploid** sperm cell, and one copy is passed from the haploid egg cell. Thus, an individual inherits two copies, one from each biological parent, for any given genomic location.

Let's look at an example in Figure 1. Here, the blue DNA on the left represents the sperm haploid genome, and the yellow DNA on the right represents the egg haploid genome. These cells come together to make an offspring, shown here as an individual with a diploid genome inherited from both the sperm and the egg.

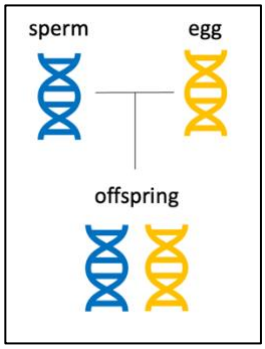


Figure 1. Haploid sperm and eggs cells come together to make a diploid offspring.

At any location in the genome, the genotype of the offspring will depend on the DNA they inherited from both biological parents. An individual inherits two copies of DNA, one from the sperm and one from the egg. Each copy, or version of DNA, is called an **allele**. At any DNA **locus**, if the two inherited alleles are the same, the individual is **homozygous** at that locus. If the alleles are different, the individual is **heterozygous**.

Let's examine one specific DNA locus in the genome that is known to contain a SNP in Figure 2. Here at the circled locus, we observe the sperm cell carries a G allele, and the egg cell carries an A allele. Since the offspring inherits one allele from each parent, the offspring's genotype is heterozygous at this locus.

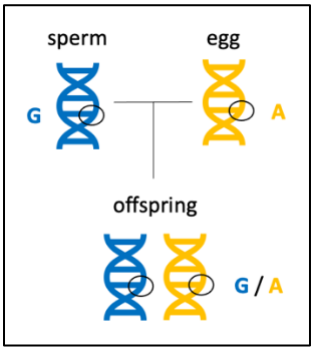


Figure 2. An offspring's genotype at one locus is determined by what alleles they inherit.

Each site of our genomes can be examined in the same way to observe which individuals carry which DNA variants. Looking at another SNP at a different DNA locus in Figure 3, we observe that here the sperm cell carries an A allele, and the egg cell carries a T allele, resulting in an offspring that is heterozygous at this locus.

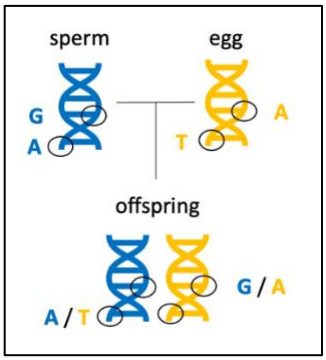


Figure 3. Different regions of the genome can carry different alleles, or variants, across individuals.

Allele Frequencies

Counting alleles in individuals reveals **allele frequencies**. This is a measure of the distribution of all DNA variations (alleles) in a **population**. It can be calculated very simply once you know the number of each allele observed in your population, as well as the total number of individuals in your population. The formula is:

$$Allele\ Frequency = \frac{v}{2N}$$

Where the **variable** v is the number of each variant allele detected in the dataset, and the variable N is the total number of diploid individuals in the dataset. Written another way without variables, the formula for allele frequency is:

$$Allele\ Frequency = \frac{Allele\ count\ of\ a\ specific\ allele\ in\ the\ population}{Total\ allele\ count\ in\ the\ population}$$

This allele frequency number can either be reported as a fraction or as a percent. To report as a fraction, the calculation ends with the formulas as shown above. To report as a percent, the number is multiplied by 100:

$$Allele\ Frequency\ (percent) = \frac{v}{2N} * 100$$

$$Allele\ Frequency\ (percent) = \frac{Allele\ count\ of\ a\ specific\ allele\ in\ the\ population}{Total\ allele\ count\ in\ the\ population} * 100$$

Let's work through an example of this by returning to our example. In Figure 4, the genomes of the two parents of the offspring are now revealed, and the genotypes at the first DNA site are shown for all three individuals.

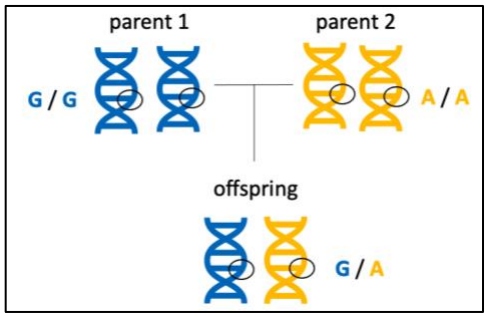


Figure 4. The genomes of the parents are revealed and the genotypes of all 3 individuals are known at this DNA site.

We can count how many of each variant allele we detect in this dataset and calculate allele frequencies for each allele at DNA site 1. Recall that at every DNA locus, there are four possible variant alleles for the four DNA nucleotides: either an A, T, C, or G will be present. In this example, there are 3 individuals total which is the population of this dataset. There are no C or T alleles. A total of 3 G alleles and 3 A alleles are present. This can be recorded in a table, like in Figure 5.

	Allele count at DNA SNP site 1
C	0
T	0
A	3
G	3

Dataset: N = 3 individuals

Figure 5. Each variant allele from Figure 5 at DNA SNP site 1 is counted and entered into the table.

Now the allele frequency fraction for each variant allele can be calculated as follows:

$$C\ Allele\ Frequency\ at\ SNP\ 1 = \frac{Allele\ count\ of\ C\ allele\ in\ the\ population}{Total\ allele\ count\ in\ the\ population} = \frac{0}{6} = 0$$

$$T\ Allele\ Frequency\ at\ SNP\ 1 = \frac{Allele\ count\ of\ T\ allele\ in\ the\ population}{Total\ allele\ count\ in\ the\ population} = \frac{0}{6} = 0$$

$$A\ Allele\ Frequency\ at\ SNP\ 1 = \frac{Allele\ count\ of\ A\ allele\ in\ the\ population}{Total\ allele\ count\ in\ the\ population} = \frac{3}{6} = 0.5$$

$$G\ Allele\ Frequency\ at\ SNP\ 1 = \frac{Allele\ count\ of\ G\ allele\ in\ the\ population}{Total\ allele\ count\ in\ the\ population} = \frac{3}{6} = 0.5$$

Remember that these allele frequencies can also be reported as percentages. The allele frequency percent for each variant allele would be:

$$C\ Allele\ Frequency\ at\ SNP\ 1 = \ 0 * 100 = 0\ \%$$

$$T\ Allele\ Frequency\ at\ SNP\ 1 = \ 0 * 100 = 0\ \%$$

$$A\ Allele\ Frequency\ at\ SNP\ 1 = \ 0.5 * 100 = 50\ \%$$

$$G\ Allele\ Frequency\ at\ SNP\ 1 = \ 0.5 * 100 = 50\ \%$$

Recall that allele frequencies represent the proportion of each DNA variant allele observed in the population. But, what is that population? In our example, we know our dataset is only 3 individuals, and they are biologically related which means they share DNA. Allele frequency data can change based on the population dataset size and the diversity of individuals.

For example, let's examine the same DNA SNP site 1 in two datasets with a different number of individuals in Figure 6. Our example with 3 individuals gives very different allele frequency numbers than looking at 50 individuals in a larger, more diverse dataset. Graphing this data as a pie chart gives us another representation of the same data, which shows clearly the drastic different in frequencies of each allele with a bigger and more diverse dataset.

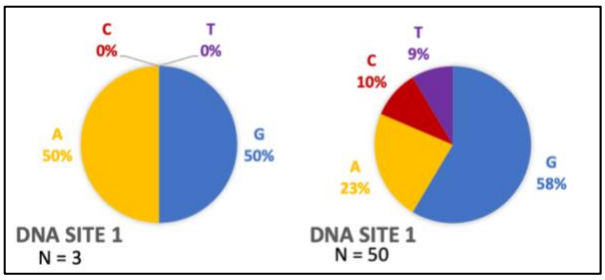


Figure 6. The allele frequencies at any DNA site can change based on the population examined.

DNA Sequencing

Ancestry testing companies typically perform this type of SNP genotyping at DNA sites with known and high variation. Interestingly, some medical tests also use similar technology to detect known variants. Whole genome sequencing is not typically performed in ancestry tests.

Spreadsheets and Tables

Spreadsheets and tables are used to display information from different analyses. Each unit of a spreadsheet or table is a **cell**, and information such as numbers, dates, or words can be entered. When information from multiple cells is arranged **vertically**, it forms a **column**. When information from multiple cells is arranged **horizontally**, it forms a **row**. **Headers** are cells with descriptions that provide additional information about what is in a row or in a column.

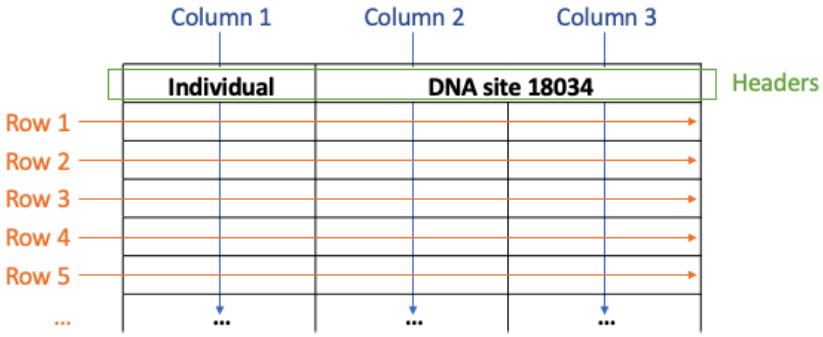


Figure 7. A table or spreadsheet has many cells of information. Columns, rows, and headers are highlighted.

We already saw an example of a table in Table 1. Each DNA nucleotide is a row with one piece of information that corresponds to it: an allele count number. The allele count number is a column, and has a descriptive header. Go back to review that table to notice the features: it has 2 columns of information, one with a header, and there are 4 rows of data.

Quick Knowledge Check

Check your understanding of the background material by answering these questions.

1. What statement best describes alleles?
    a. Haploid gamete cells with a single set of chromosomes.
    b. Two alternative forms of a gene that arose from DNA variations.
    c. Diploid genomes with two sets of chromosomes.
    d. Individuals with various genotypes in a population.

2. True or false? Allele frequency calculations must be calculated for each allele separately.

3. Draw a table with 2 columns and 3 rows. How many cells total are in this table?

Activity

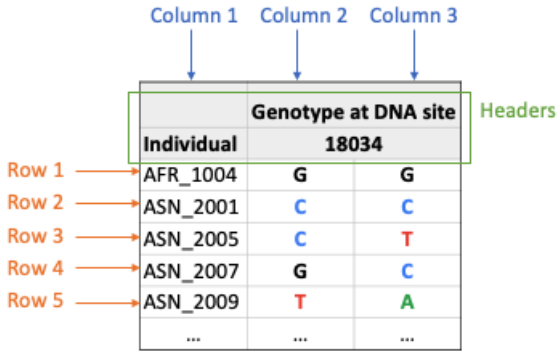
Dr. V shows Sam and the rest of the class an example of an ancestry testing company called *23Chromosomes* that is building a reference DNA database. *23Chromosomes* selected 50 individuals who volunteered to share their genetic information with the company. These carefully selected individuals represent 5 populations from around the world: African, Asian, European, Native American, and Pacific Islander. *23Chromosomes* will use the genetic data from these individuals to build their own DNA **reference database**.

Follow along with Dr. V's example to analyze the data from *23Chromosomes* and learn how DNA ancestry tests work. Calculate the allele frequencies for different alleles across populations and identify which alleles are associated with which populations.

Part 1. Explore the data

The genomic technologies division of *23Chromosomes* performed SNP genotyping on 50 individuals from 5 regions around the world. They delivered the genotype data in spreadsheets and sent it to the computational biology team for analysis.

First, let's observe part of the data in the spreadsheets you chose to learn how it is organized. This image shows part of Table 1 for DNA Site 18034, with the rows, columns, and headers identified. Use this table shown to answer the questions that follow.



a. Record the name of the Column 1 header.

b. How many individuals are displayed in the portion of the table shown?

c. The individuals are distinguished from one another by a 3-letter code, an underscore, and a 4-number code. Based on what you know about the origin of this data, what do the 3 letters represent?

d. Which geographic regions are represented in the individuals shown in this part of the table?

e. Record the name of the header for Columns 2 and 3.

f. Why are there two columns for this header?

g. Record the genotype for the individual in Column 1, Row 1.

h. Choose another individual and record their information:
Population:
Individual number:
Genotype at DNA site 18034:

Part 2. Organize the data

Now that we're more familiar with the data, it's time to start working with the data from *23Chromosomes*.

Find all data from *23Chromosomes* in the linked Google Spreadsheets. There are five spreadsheets, each with genotype data from one of the five DNA sites (SNPs) in all 50 individuals. There is also one master spreadsheet with all of the data. Choose one of the five DNA sites to start and focus on **Table 1 Genotype Data**.

23Chromosomes DNA Site 18034
23Chromosomes DNA Site 46754
23Chromosomes DNA Site 53134
23Chromosomes DNA Site 95005
23Chromosomes DNA Site 123030
- or -
23Chromosomes All Data

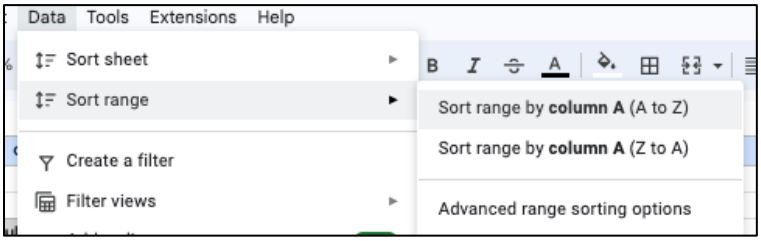
Table 1 contains the genotype data from 50 individuals in all five populations at one DNA site. This data is not organized. Your first task is to sort the table named Table 1 so that the individuals are grouped by population.

One approach is to select the data in the table and use a spreadsheet feature called sort. Using your cursor or mouse, select all of the individuals and all of the genotype data. Do not select any of the headers. Make sure you scroll and capture all the data that may be outside of your current view!

5	**(1) First, organize Table 1 based on population.**		
6			
7	**Table 1. Genotype data**		
8			
9		**Genotype at DNA site**	
10	**Individual**	**18034**	
11	AFR_1004	G	G
12	ASN_2001	C	C
13	ASN_2005	C	T
14	ASN_2007	G	C
15	ASN_2009	T	A
16	EUR_3002	G	G
17	EUR_3009	C	A
18	NAM_4001	A	T

In Table 1, select all of the individual and genotype data, not the headers.

Navigate to the top menu Data, then select Sort range, then select Sort range by column A (A to Z).



Sort the selected data range.

Now look back at Table 1. You should see the data changed in the table. To check and ensure you sorted properly, find the individuals whose information you recorded previously. Are their genotypes the same? If yes, then you sorted properly! If not, try again by going back to the original spreadsheet.

Part 3. Count alleles

The genotype data in Table 1 should now be organized with all individuals grouped by population. Now, the alleles for all individuals can be counted more easily.

In your spreadsheet, find **Table 2 Allele Count Data** for the DNA site you are working on. Next, use the sorted Table 1 to count each allele, for the given DNA site, in each population. Record your results in Table 2. Continue counting each variant for all 10 individuals in the population. Repeat this for all five regions. Total your counts and enter them into the appropriate cells in Table 2.

Part 4. Calculate allele frequency

Now that you calculated how many variants are detected in the individuals at each DNA site, you can calculate the allele frequency, or the proportion of each variant, in each population.

In your spreadsheet, find **Table 3 Allele Frequency Percent Data** for the DNA site you are working on. Use the allele count data you previously generated in Table 2 to calculate the allele frequency percent in each population.

Recall that the formula to calculate allele frequency percent is:

$$Allele\ Frequency = \frac{Allele\ count\ of\ a\ specific\ allele\ in\ the\ population}{Total\ allele\ count\ in\ the\ population} * 100$$

Continue your calculations for each variant for all 10 individuals in each population. Repeat this for all five regions. Record your results in the appropriate cells in Table 3.

Part 5. Compare allele frequency data

Look at the allele frequency data from all five DNA sites in all five populations. First, compare the numbers for the allele frequencies at one DNA site across all populations. Then, compare the numbers for allele frequencies in one population across all DNA sites. What do you notice? Choose at least three of the following questions and record your answers below.

1. What biological concepts can explain these observations?

2. Why don't all individuals from the same population have the same genotypes?

3. Why do some populations have the same frequencies at some DNA sites?

4. Would you expect a different ancestry testing company to have the same allele frequency data for these populations?

5. What would the data look like if we had 500 individuals? What about 500,000 individuals?

6. What would make you more confident in the data?

Part 6. Ethics

The company *23Chromosomes* used data from individuals from 5 populations: African (AFR), Asian (ASN), European (EUR), Native American (NAM), and Pacific Islander (PIS).

Using the map provided, circle and label the areas that correspond to each region. If you're in a group or class, work independently, then compare your answers with your peers when everyone has finished. Then choose at least three of the following questions and record your answers below.

1. If you compared with your peers, did you have different answers? Which version is correct?

2. What areas of the world are not covered?

3. What about countries that span more than one continent?

4. How did you define Asian? Native American? European?

5. How large is each region?

6. How many modern-day countries are in each region?

7. How would you have defined these regions 100 years ago? How might these regions change 100 years from now?

Part 7. Careers

Explore jobs and career paths that relate to this activity.

1. Navigate to any job search site. Some recommended ones are
   - Indeed: https://www.indeed.com/salaries
   - Zippa: https://www.zippia.com/careers
   - JobViz: https://www.galacticpolymath.com/jobviz

2. Search for the jobs from this activity. You can also find more jobs using keywords from the activity or explore jobs and categories on the site.

   Bioinformaticians analyze genomic data. Similar jobs include Data Scientist and Bioinformatics Analyst.

   Genomic Technologists perform DNA sequencing assays. Similar jobs include Laboratory Technician and Research Technician.

   Population Geneticists study the genetics of groups of individuals, like humans. Similar jobs include Computational Geneticist and Statistical Geneticist.

3. Fill in the table below with 2 jobs that interest you. Record the job title, degree(s) and training needed, and the salary estimate. You can also write a description of the work and any other notes about why you found the job interesting. Continue filling the table with more jobs if you want to.

Job title	Degree(s)/training needed	Salary estimate	Description of work	Notes

4. Hear from people in some of the jobs you just discovered. Choose 1 resource, then use the table below to record the resource you explored, as well as your thoughts about the people and the jobs they do. Continue filling the table with more jobs if you want to.
    - JAX Career Chats: Bioinformatics Analyst
    - JAX Career Spotlight: Genomic Technologist
    - I Am A Scientist: Population Geneticist

Resource you explored	Person name and job title	In your own words, describe the work they do	Which of their traits match your skills and interests?	What do you want to learn more about?

Glossary

Allele – One of several alternative forms of a gene. Alleles for a given gene have different DNA sequences, which can lead to different phenotypes. In a diploid cell, each cell has two alleles for each gene (one from each parent). These two alleles will be found at the same position (locus) on homologous chromosomes.

Allele frequency – The fraction of all chromosomes in a population that carry a specific allele over the total population.

Cell – In a spreadsheet or table, a cell is one unit where information such as numbers or words can be entered.

Column – In a spreadsheet, when information from multiple cells is arranged vertically.

Deoxyribonucleic acid (DNA) – A biological molecule of which the primary role is the storage of genetic information. DNA is made of deoxyribonucleotides. The nitrogenous bases found in DNA include adenine (A), guanine (G), cytosine (C) and thymine (T).

Gamete – A gamete is a reproductive cell of an animal or plant, such as egg and sperm cells. In animals, these cells are haploid and carry only one copy of each chromosome.

Genome – The complete set of chromosomes, or genetic material, of an organism or cell.

Genotype – The genetic makeup of an organism (whereas the term phenotype describes the physical traits of an organism). The term genotype can be used to describe which alleles an individual has for a single gene. When describing one particular gene, genotype refers to the pair of alleles inherited by the organism for that gene. The term genotype can also be used to describe the complete set of a cell's or an organism's genes. For example, humans have about 20,000 genes, so a genotype would indicate which alleles are present for each of those genes.

Header – In a spreadsheet, cells that have descriptions that provide additional information about what is in a row or column.

Homozygous – Having two identical alleles for a given gene (ie, the same allele was inherited from each parent).

Horizontal – A direction that is parallel to the plan of the horizon, at right angles to the vertical.

Locus – A locus in genomics is a physical location within the genome. It can be a region like a gene or portion of a gene, or a specific nucleotide or set of nucleotides.

Nucleotide – The building blocks of nucleic acids (DNA and RNA) comprised of a nitrogenous base, five-carbon sugar, and phosphate.

Phenotype – The observable characteristics of a cell or organism.

Population – In biology, a population is the total number of individuals in a specific area.

Reference genome – A template genome for organism. This genetic resource is a digital nucleic acid sequence database, assembled by scientists as a representative example of the genomic features in one idealized individual.

Row – In a spreadsheet, when information from multiple cells is arranged horizontally.

Sequencing – Sequencing is a technique that is used in molecular biology to determine the order of nucleotides in a particular DNA or RNA molecule. It involves identifying the specific order of nucleotides that make up the molecule, which can provide important information about the genetic code of an organism. Sequencing can be done using a variety of methods, including Sanger sequencing, next-generation sequencing, and single-molecule sequencing.

Single nucleotide polymorphism – A single nucleotide polymorphism (abbreviated as SNP, pronounced as *snip*) is a type of genomic variant when one single nucleotide in the DNA is changed. Also known as a single nucleotide variant (abbreviated as SNV).

Variable – In mathematics, a variable is a symbol (such as v, N, or x) that represents an object (such as a number).

Variant – A change or difference in the DNA sequence of a cell or organism.

Vertical – A direction where the top is directly above the bottom, at right angles to the horizontal.

Implementation Strategies

Coming soon.

NGSS Alignments

Coming soon.

Supporting Materials

Coming soon.

Feedback

Did you use the Ancestry Testing content in your class(es)? If so, we'd love to hear how it went. Use the following form to provide the TtGG team with feedback:

Feedback Form

Questions? Email ttgg@jax.org