

## Teacher Guide: SNP Analysis and Pharmacogenetics

### ACTIVITY OVERVIEW

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**Abstract:**

Students learn about Single Nucleotide Polymorphisms (SNPs) in DNA sequences and how they can be used to match patients with appropriate medications. Students locate the SNPs in DNA sequences for fourteen patients, categorize them into haplotypes (same SNPs), and prescribe a medication to a fictitious patient based on their DNA sequence.

**Module:**

Pharmacogenomics: Drugs Designed for You

**Key Concepts:**

Single Nucleotide Polymorphisms (SNPs); a group of people who share the same SNPs are known as a haplotype; different haplotypes may respond differently to medications; medications may be prescribed based on haplotype

**Prior Knowledge Needed:**

DNA bases; DNA sequence

**Materials:**

Student pages  
Highlighter  
Scissors

**Appropriate For:**

Ages: 12 - 20  
USA grades: 7 - 14

**Prep Time:**

45 minutes to review and copy

**Class Time:**

30 minutes

**Activity Overview Web Address:**

<http://gslc.genetics.utah.edu/teachers/tindex/overview.cfm?=194>

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Other activities in the ***Pharmacogenomics: Drugs Designed for You*** module can be found at: <http://gslc.genetics.utah.edu/teachers/tindex/>

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## Teacher Guide: SNP Analysis and Pharmacogenetics

### I. PEDAGOGY

#### A. Learning Objectives

- Students will learn about a key Pharmacogenetic approach to tailoring prescription medication to an individual's genotype.
- Students will learn that single nucleotide substitutions in DNA sequences are known as Single Nucleotide Polymorphisms (SNPs).
- Students will locate SNPs in genetic sequences.
- Students will learn that people with the same SNPs in a particular region of DNA are grouped into haplotypes.
- Students will group DNA sequences into haplotypes based on the SNPs those sequences contain.
- Students will learn that people with different haplotypes may have a different response to the same medication.

#### B. Background Information

One of the goals of pharmacogenetics is to correlate variation in drug response to genetic variation. The most common type of variation in DNA is a single base substitution, known as a Single Nucleotide Polymorphism (SNP). For example, an adenine in one sequence of DNA is placed where a cytosine is located in another. Because SNPs tend to be inherited in groups, scientists can break a larger population into sub-groups, called haplotypes, based on the SNPs those individuals possess. The hope is to correlate differences in drug response and disease risk to haplotype groups.

SNPs occur roughly once in every 300 base pairs. This means there are 10 million SNPs in the entire genome (genome = 3 billion nucleotides). In order to be classified as a SNP, the substitution must occur in at least 1% of the population. Most SNPs occur outside of genes and therefore have no effect on genes or their protein products; these are known as *linked SNPs*. SNPs located within genes are called *causative SNPs* and fall into two categories: coding and non-coding. Coding SNPs change the protein product of the gene, and non-coding SNPs, which are located in the regulatory sequence of the gene, affect how much protein is produced from the affected gene.

SNPs tend to be inherited in groups. These groups of SNPs and their various possible combinations are known as *haplotypes*.

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For example:

Haplotype One: c t t g g a c t g a t

Haplotype Two: c t g g g a t t g c t

The field of pharmacogenetics aims to define haplotype groups and use them in the following ways: (a) correlate haplotypes to drug response for particular medications and (b) correlate haplotypes to risk for particular diseases.

If pharmacogenetics is successful, in the future a physician may first determine to which haplotype group a patient belongs, and then prescribe a course of treatment based on which medications and dosages are most successful with that haplotype.

### C. Teaching Strategies

#### 1. Timeline

- One day before activity:
  - Make copies of student pages S-1 to S-4, enough for each student
  - Collect necessary materials (see Materials List)

Note: You may wish to read the activity directions (pages S-1 to S-2) aloud to the class instead of providing each student with a copy. In that case copy only pages S-3 to S-4 for each student to work with.

- Day of activity:
  - Carry out the activity as described in the activity instructions on pages S-1 to S-3

#### 2. Invitation to Learn

- To engage students in the topic of pharmacogenomics, carry out the *Wanna Buy Some Drugs? Print-and-Go™* activity from the *Pharmacogenomics: Drugs Designed for You* module available on the Genetic Science Learning Center Website at: (<http://gslc.genetics.utah.edu/teachers>)

#### 3. Classroom Implementation

- Begin class by asking the class the following questions:
  - Are any of you allergic to any medications?
  - Have you ever had an adverse reaction to a medication?
  - Have you ever taken a medication that didn't work that well?

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- Inform the class that:
  - People respond differently to medications.
  - Each year, 106,000 Americans die from adverse drug reactions and 2.2 million suffer serious side effects; others have no problems at all.
  - Scientists, physicians and the pharmaceutical companies think that variation in response to drugs could be due to genetic variation.
  - A new field called *pharmacogenetics* is emerging that aims to figure out how an individuals' genetic make-up might correlate to their reaction to specific drugs.
  - If pharmacogenetics is successful, in the future a physician might prescribe a course of treatment based on an individuals' genotype. In order to make this a reality, scientists are endeavoring to group people into categories (called haplotypes) based on differences in their genotype and to correlate the response to specific medications for each category. Today's activity highlights how scientists might do this.
- Hand out the student pages (S-1 to S-4), highlighters and scissors to the students. Instruct them to follow the directions to carry out the activity.

### 4. Extensions

- For reinforcement, have students visit *SNiPping Away at the Problem*, an online activity in the *Pharmacogenomics: Drugs Designed for You* module on the Genetic Science Learning Center website (see **Additional Resources**). Pay particular attention to the *Making SNPs Make Sense* animation that is part of this piece.
- This activity uses the drug albuterol as an example. Students may find information about how albuterol works on the cellular level, as well as how many different haplotypes are currently being compared against albuterol effectiveness in the *Making SNPs Make Sense* animation on the *SNiPping Away at the Problem* page in the *Pharmacogenetics: Drugs Designed for You* module on the Genetic Science Learning Center website (see **Additional Resources**)

### 5. Adaptations

- Provide only pages S-3 and S-4 for students to work with while you read the instructions contained in S-1 to S-2 aloud to the class.
- If highlighters are not available, students may use pen, pencil or colored pencil to circle or underline the SNP locations in the DNA Sequence Data (page S-4).

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### 6. Assessment Suggestions

- Collect page S-3 as an assessment of student understanding. See **Teacher References** for an answer key.

### 7. Common Misconceptions

- SNPs are sometimes confused with disease-causing mutations. They are different in the following ways:
  - Many SNPs are located outside of genes and therefore have no effect on any protein product.
  - To be classified as a SNP, the nucleotide substitution must occur in at least one percent of the population. No disease-causing mutation is this common.

## II. ADDITIONAL RESOURCES

### A. Activity Resources linked from the online Activity Overview at:

<http://gslc.genetics.utah.edu/teachers/tindex/overview.cfm?id=activity>

- Website: *SNiPping Away at the Problem* - Students learn about Single Nucleotide Polymorphisms (SNPs) and how they might be used in the future to plan the course of treatment for medical patients.

## III. MATERIALS

### A. Detailed Materials List

- Student handout (S-1 to S-4)
- Highlighters
- Scissors

## IV. STANDARDS

### A. U.S. National Science Education Standards

#### Grades 5-8:

- Content Standard C: Life Science - Reproduction and Heredity; the characteristics of an organism can be described in terms of a combination of traits. Some traits are inherited and others result from interaction with the environment.

#### Grades 9-12:

- Content Standard C: Life Science - Molecular Basis of Heredity; in all organisms, the instructions for specifying the characteristics of an organism are carried in DNA.
- Content Standard F: Science in Personal and Social Perspectives - Personal

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and Community Health; many diseases can be prevented, controlled or cured.

### **B. AAAS Benchmarks for Science Literacy**

#### Grades 9-12:

- The Human Organism: Physical Health - new medical techniques, efficient health care delivery systems, improved sanitation, and a fuller understanding of the nature of disease give today's human beings a better chance of staying healthy than their forebears had.
- The Designed World: Health Technology - knowledge of genetics is opening whole new fields of health care.

### **C. Utah Secondary Science Core Curriculum**

#### *Intended Learning Outcomes for Seventh and Eighth Grade Integrated Science*

Students will be able to:

5. Demonstrate Awareness of the Social and Historical Aspects of Science
  - a. Cite examples of how science affects life.

#### *Intended Learning Outcomes for Biology*

Students will be able to:

5. Demonstrate Awareness of the Social and Historical Aspects of Science
  - a. Cite examples of how science affects human life.

#### Biology (9-12)

Standard 4: Students will understand that genetic information coded in DNA is passed from parents to offspring by sexual and asexual reproduction. The basic structure of DNA is the same in all living things. Changes in DNA may alter genetic expression.

Objective 3: Explain how the structure and replication of DNA are essential to heredity and protein synthesis

- f. Research, report, and debate genetic technologies that may improve the quality of life (e.g., genetic engineering, cloning, gene splicing).

### **V. CREDITS**

#### **Activity created by:**

Molly Malone, Genetic Science Learning Center

Pete Anderson, Genetic Science Learning Center (illustrations)

#### **Funding:**

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## Teacher References: SNP Analysis and Pharmacogenetics Answer Key

### Step 4: Prescribing Medication Based on Genetic Code

A patient comes in to a doctors' office complaining of shortness of breath when she exercises for long periods of time. The doctor diagnoses the patient with exercise-induced asthma. Before prescribing medication however, the doctor analyzes a sample of the patient's DNA and determines that the patient is in Haplotype group d. Based on your research, would you recommend albuterol for this patient?



No

Why or why not?

Albuterol has no effect on this haplotype

### Haplotypes Table

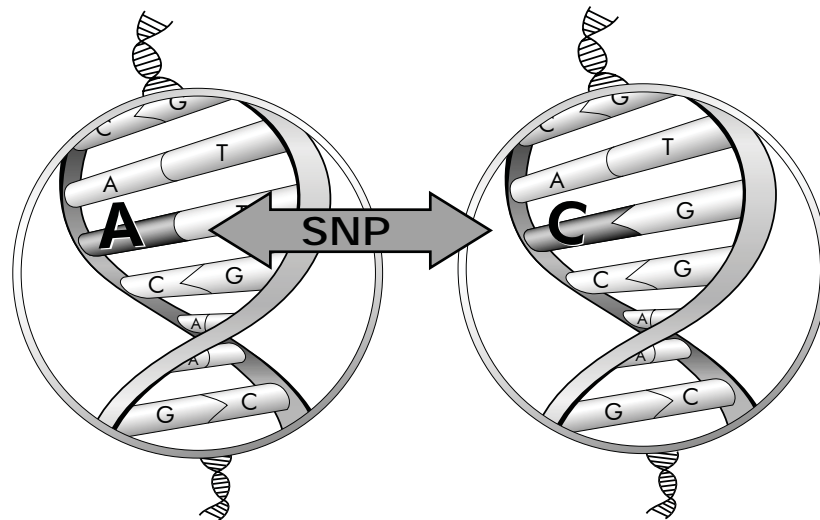
Haplotype #	Highlighted SNPs	Patient #'s	Results of the Study
a	TAT	4,7	○
b	TAG	1,10	✓
c	TGT	8,14	✓
d	CAG	9,3	○
e	CGG	12,2	✓
f	TGG	5	✓
g	CGT	13,6	∅
h	CAT	11	✓



## SNP Analysis, Haplotypes and Pharmacogenetics

DNA sequences in humans are 99.9% the same. That means that 0.1% of the human DNA sequence varies from person to person. Scientists think that this genetic variation leads to differences in how individuals respond to drugs.

Read and follow the steps below to learn how scientists are analyzing DNA in the hope of one day being able to tailor prescriptions to individuals based on their genetic code.



You will need:

- Genetic sequence data for 14 patients (page S-4),
- A highlighter or colored pencil
- Scissors

### Step One: Locate SNP Locations in a Region of DNA

Scientists have found that many DNA variations are single nucleotide substitutions, also known as Single Nucleotide Polymorphisms (SNPs). Follow these steps to find the location of the SNPs in the genetic sequence data (page S-4) of your patients:

1. Compare Patient #1 and Patient #2. Highlight or underline any SNPs in each row.
2. Compare Patient #2 and Patient #3. Highlight or underline any SNPs in each row.
3. Repeat, comparing #3 and #4, #4 and #5, and so on until you have compared all rows.
4. Use your highlighter or colored pencil to draw vertical columns through all the rows that connect the SNP locations you've highlighted or underlined.

Example:








C	T	GACTA	A	G
C	C	GACTA	G	G
C	C	GACTA	A	G

### Step Two: Create Haplotype Groups

By looking at a number of SNPs in a particular region of DNA, scientists can group people into what are known as Haplotypes. People with the same SNPs in that region are placed in the same haplotype group. Group your patients into haplotypes:

1. Cut out each patient's row of genetic sequence data.
2. Group patients whose highlighted SNPs are the same. (Be sure that all three highlighted letters are the same!)
3. Fill in the "Patient #'s" column on the Haplotypes Table (Page S-3)

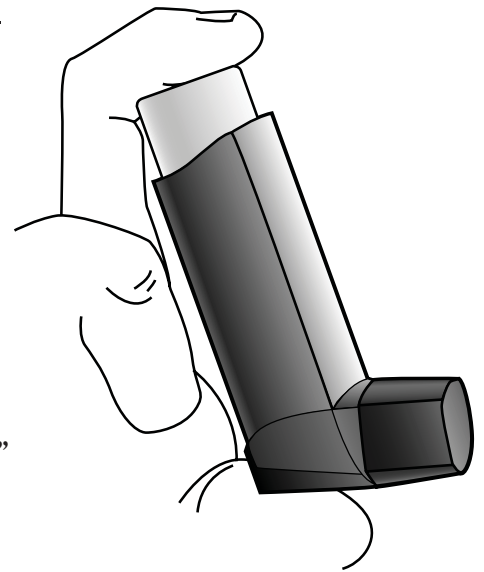
Example:

<u>Haplotype "x"</u>			<u>Haplotype "y"</u>			<u>Haplotype "z"</u>		
Patient 002			Patient 001			Patient 003		
Patient 005			Patient 004			Patient 007		
Patient 006								

### Step 3: Testing Haplotype Response to Albuterol

Albuterol inhalers are commonly prescribed for asthma. However, the reaction to and efficacy of albuterol varies. Some people (✓) respond very well to the drug - their asthma symptoms are relieved. Some people (○) don't respond at all to the drug - their symptoms persist and they must try another medication. Some people (∅) unfortunately, have an adverse reaction to the drug - they become even more ill than they were to begin with.

You run a study (described below) examining the reaction to albuterol for each of the haplotypes you've identified. Record your findings in the "Results of the Study" column of the Haplotypes Table:



#### Study Results

1. People in **haplotype groups b, c, e, f, and h** responded well to albuterol. Place a ✓ in the "Results of the Study" column for each on the Haplotypes Table.
2. People in **haplotype groups a and d** showed no improvement with albuterol. Place a ○ in the "Results of the Study" column for each on the Haplotypes Table.
3. People in **haplotype group g** had an adverse reaction to albuterol. Place a ∅ in the "Results of the Study" column for this group on the Haplotypes Table.

Step 4: Prescribing Medication Based on Genetic Code

A patient comes into a doctor's office complaining of shortness of breath when she exercises for long periods of time. The doctor diagnoses the patient with exercise-induced asthma. Before prescribing medication, however, the doctor analyzes a sample of the patient's DNA and determines that the patient has Haplotype group 'd'. Based on your research, would you recommend albuterol for this patient?



\_\_\_\_\_

Why or why not?

\_\_\_\_\_

Haplotypes Table

Haplotype	Highlighted SNPs	Patient #'s	Results of the Study
a	TAT		
b	TAG		
c	TGT		
d	CAG		
e	CGG		
f	TGG		
g	CGT		
h	CAT		

## DNA Sequence Data

Patient 1 CTGACTAAGTACCGA

Patient 2 CCGACTAGGTACCGA

Patient 3 CCGACTAAGTACCGA

Patient 4 CTGACTAAGTACCTA

Patient 5 CTGACTAGGTACCGA

Patient 6 CCGACTAGGTACCTA

Patient 7 CTGACTAAGTACCTA

Patient 8 CTGACTAGGTACCTA

Patient 9 CCGACTAAGTACCGA

Patient 10 CTGACTAAGTACCGA

Patient 11 CCGACTAAGTACCTA

Patient 12 CCGACTAGGTACCGA

Patient 13 CCGACTAGGTACCTA

Patient 14 CTGACTAGGTACCTA