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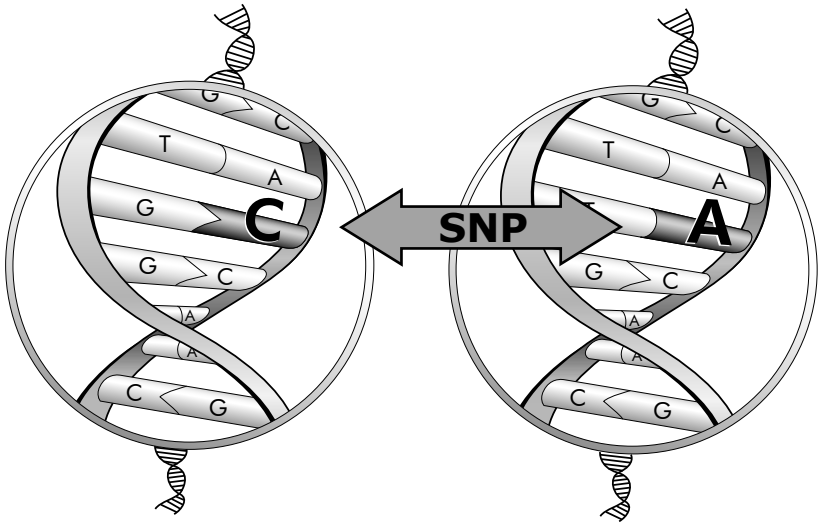
SNP Analysis, Haplotypes and Pharmacogenetics

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

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Step Two: Create Haplotype Groups

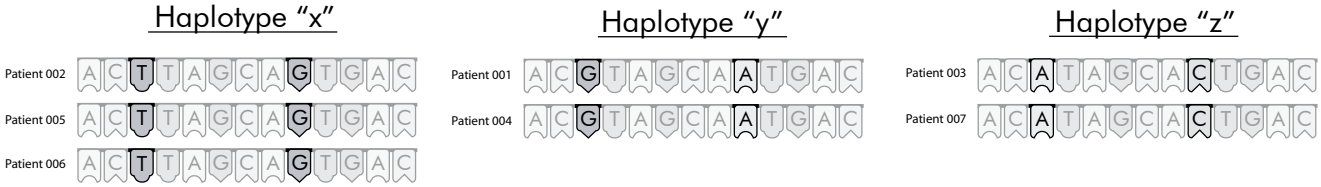
By looking at a number of SNPs in a particular region of DNA, scientists can group people into what are known as Haplotypes. People with the same SNPs in that region are placed in the same haplotype group. Group your patients into haplotypes:

5. Cut out each patient's row of genetic sequence data.

6. Group patients whose highlighted SNPs are the same. (Be sure that all three highlighted letters are the same!)

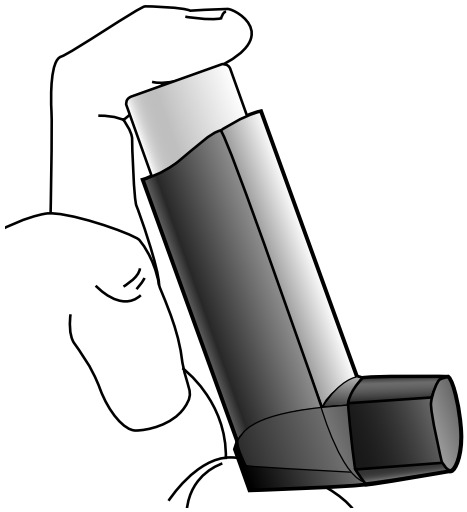
7. Fill in the "Patient #'s" column on the Haplotypes Table (Page 3)

Example:



Step Three: 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 (**O**) 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

- 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.
- People in haplotype groups a and d showed no improvement with albuterol. Place a **O** in the "Results of the Study" column for each on the Haplotypes Table.
- People in haplotype group g had an advese reaction to albuterol. Place a **-** in the "Results of the Study" column for this group on the Haplotypes Table.

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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	Result 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