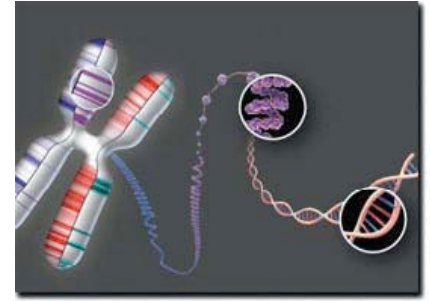


# **“SNPs and snails and puppy dog tails, and that’s what people are made of ...” A Case Study on Genome Privacy**



by

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***Study questions 1-4 (parts A and B) due Beginning of Class Wednesday, November 8<sup>th</sup>***

## ***Objectives***

After completing this case study, you will be able to:

- Define the term SNP and list three uses of SNP technology.
- Design an experiment to identify SNPs.
- Describe a potential privacy issue associated with SNP technology.
- Explain the current status of genome privacy laws.
- Apply scientific reasoning skills to an ethical issue in science.
- Write a letter to your United States Representative for/against amending the Genetic Information Nondiscrimination Act.

## ***Scenario, In Class on Friday, November 10<sup>th</sup>***

Various lobbyists and representatives of interest groups will present background information to a mock U.S. House of Representatives Health, Employment, Labor, and Pensions Subcommittee (a subcommittee of the Committee on Education and Labor) as they consider voting to amend the Genetic Information Nondiscrimination Act, or GINA (<http://thomas.loc.gov/cgi-bin/bdquery/z?d110:HR00493:#>). The Subcommittee is voting on whether or not to amend the law to include protection for individuals in the military and to prohibit life, disability, or long-term-care insurers from using a person’s genetic information in determining eligibility or premiums.

## ***Follow up Assignment, Due 4:30 pm Saturday, November 11<sup>th</sup> on Moodle***

Write a letter to your U.S. Representative that is either in support of passing or shelving an amendment to the Genetic Information Nondiscrimination Act. Give substantiated reasons for your position based on your readings and our class discussions. If you are not a U.S. citizen, please write to the local U.S. Representative.

To find contact information for your representative: <http://www.house.gov/representatives/find/>

## ***SNP Overview***

*In April 1999 Terri Seargent went to her doctor with slight breathing difficulties. A simple genetic test confirmed her worst nightmare: she had alpha-1 deficiency, meaning that she might one day succumb to the same respiratory disease that killed her brother. The test probably saved Seargent's life—the condition is treatable if detected early—but when her employer learned of her costly condition, she was fired and lost her health insurance.*

This story, quoted from an article in Scientific American (“Pink Slip in Your Genes”), illustrates the potential, both good and bad, of our ever-increasing store of genetic information. In the case of Terri Seargent, she had one specific test for one known disorder. SNPs, however, present a new problem; they have the potential to quickly provide genetic information about many disorders.

What are SNPs? SNP (pronounced “snip”) stands for **single nucleotide polymorphism**. Polymorphism refers to the presence of more than one allele of a gene in a population. This allele must be present in more than 1% of the population to distinguish it from a mutation. A SNP is a specific type of allele caused by a small genetic change, or variation, that occurred generations ago within a DNA sequence. The replacement of one single nucleotide with any one of the other three nucleotides resulted in a SNP. A SNP is the simplest kind of polymorphism, because it involves a change in only one nucleotide.

The following is one example of a mutation that may have occurred long ago over evolutionary time. Originally, one DNA segment on a chromosome read GGTAAC. The replacement of the second G with a C created a novel DNA segment that reads GCTAAC. Because this variation persisted and was passed on to more than 1% of the population, it resulted in a SNP. This particular variation is referred to as a G/C SNP. Each individual in the population inherits one version of the SNP on each of the chromosomes donated by each parent. Each SNP variant, or allele, that occurs at a particular site on a chromosome is shared by some fraction of the population.

There are 10 million SNPs in the human genome (about one every 300 bp) and it is estimated that a small fraction of them, about 60,000, are found within regions of DNA that code for proteins. A single nucleotide change in the DNA sequence of a chromosome has the potential to alter the codon at that site. Codons are like words made of three nucleotides that code for a particular amino acid. A codon with a SNP has the potential to direct the cell's machinery to add a different amino acid at this site during protein synthesis. The substituted amino acid may alter either the protein's stability or function. In this manner, SNPs may be responsible for many of the phenotypic differences between humans. The majority of SNPs, however, occur in noncoding regions of the DNA and are not responsible for any protein changes.

## ***How Are SNPs Detected?***

After isolation of DNA from an individual, SNPs can be detected by first amplifying DNA in the region of interest using the polymerase chain reaction, or PCR (see <http://www.dnalc.org/ddnalc/resources/pcr.html>). To identify the nucleotide polymorphism, PCR is followed by DNA sequencing (<http://www.dnalc.org/ddnalc/resources/cycseq.html>). Recently, newer methods for identifying SNPs include the use of special DNA microarrays (we'll learn about these in class soon) called SNP microarrays (or “SNP chips”).

## ***Study Questions Part A***

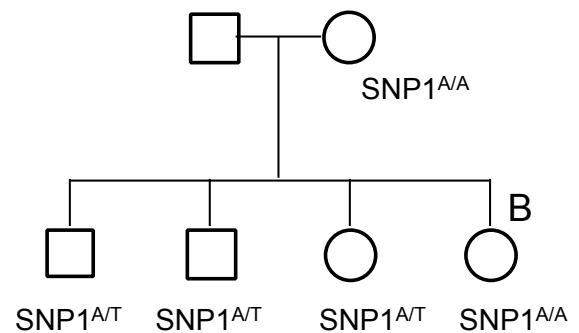
Read these questions carefully and answer thoroughly for full credit. You will need to use information covered in the course and from previous problems.

1. Look back at the genetic code table. Look carefully at the first, second, and third nucleotide in the

codons for the amino acid Arg (arginine). At what position in a codon is a SNP least likely to code for a new amino acid?

2. To the right is a pedigree showing the inheritance of a SNP (SNP1) in a biological family. This SNP is not located in a gene, and is not associated with a disease phenotype.

- How many versions of the SNP does child B have?
- What is Dad's most likely SNP genotype?
- An allele is traditionally defined as one of several alternative forms of a gene. When talking about SNPs, researchers often refer to SNP "alleles." How would you expand the definition of "allele" to include SNPs?



### ***How Are SNPs Being Used?***

SNPs can serve as genetic markers for disease. In order to establish a link between a SNP and a specific disease, the genomes of many different individuals need to be scanned for SNPs. Several SNPs are identified within the individual and a SNP profile is constructed. The identified SNPs are also recorded in web-based databases. To determine whether a particular SNP is associated with a disease, the SNP pattern found in individuals affected with the disease is compared to the SNP pattern found in unaffected individuals. A SNP may be associated with disease susceptibility if one pattern is found to be significantly more common in the affected population than in the control group. In some cases, a disease-linked SNP has already been identified and a screening test for the disease based on the SNP has been developed. Information about an individual's SNP profile may indicate whether one is at an increased risk, for example, of developing heart disease. With knowledge that they have the disease-linked SNP, the individual may choose to modify their lifestyle or take medications to prevent the disease rather than waiting for symptoms to occur. However, SNPs can also identify other diseases for which there is no effective prevention or treatment, such as Huntington's. It is important to note that although SNPs may serve as genetic markers for a disease, the majority of SNPs are not responsible for causing the disease.

It may theoretically become possible to scan one's entire genome for all SNPs. A complete genome SNP profile could indicate a whole range of diseases to which one is predisposed. Currently, the cost of sequencing every individual's genome is prohibitive. Glyn Moody, author of *Digital Code of Life: How Bioinformatics is Revolutionizing Science, Medicine, and Business*, wrote in 2004, "with a dozen companies racing towards the goal of the sub-\$1000 genome, the day when your DNA is sequenced and burnt onto a CD-ROM for roughly the cost of a conventional health checkup is not far off" (*The Guardian*, April 15, 2004). Now, the cost of sequencing a human genome is very close to \$1000 (<https://www.genome.gov/27565109/the-cost-of-sequencing-a-human-genome/>). And one company is working on getting that cost down to \$100 (<https://techcrunch.com/2017/01/10/illumina-wants-to-sequence-your-whole-genome-for-100/>).

While the cost of sequencing the whole genome has not yet reached \$100, you may have heard that companies like 23andMe (<https://www.23andme.com/>) and AncestryDNA (<https://www.ancestry.com/dna/>) are offering whole-genome scans for as little as \$99. These scans are not whole-genome sequencing, but instead use technology called a SNP microarray (or "SNP chip") to identify genetic variants, including SNPs, in the genome. As of 2016, the Ancestry DNA test scans 700,000 markers. This may sound like a lot, but

given that there are 3 billion nucleotides in the human genome, it represents a small fraction (0.02%) of the genome.

SNP profiles can be used in medicine beyond identifying disease risk. One hot area in pharmaceutical research is the design of personalized drug treatments based on a patient's SNP profile. Individuals always vary in their response to medication both in terms of effectiveness and side effects. SNP information could allow drug therapy to be customized; SNPs may provide information about the most appropriate drug to prescribe or the optimal dose. For example, an A/G SNP is found in the morphine receptor in humans. Individuals homozygous for one SNP allele are known to need much higher levels of morphine-derived pain relieving drugs. Development of a SNP screening test will allow treatment of those individuals with the appropriate dose of morphine.

In addition to medical uses, SNPs are proving useful in mapping the migrations of human populations. SNPs provide information about human evolution and the descent from ancestral populations (see, for example, "Ancient DNA Could Unravel the Mystery of Prehistoric European Migration," from *Smithsonian.com*, June 2017, available at <https://www.smithsonianmag.com/science-nature/ancient-dna-could-unravel-mystery-prehistoric-european-migration-180963702/>).

### ***Challenge Study Questions Part B***

Read these questions carefully and answer thoroughly for full credit. You will need to use information covered in the course and from previous problems.

3. Explain two distinct mechanisms for how a SNP that does not change a protein's sequence can still be associated with a disease. Hint: think about how a gene is composed of both regulatory and interrupted coding regions (i.e. exons and introns).
4. The substitution of a T for an A in the protein coding sequence of the hemoglobin beta chain gene introduced a SNP. This SNP changed the amino acid incorporated into the hemoglobin beta chain, resulting in the disease symptoms of sickle cell anemia. Unaffected individuals have the DNA sequence GAGGAG, in their hemoglobin beta chain gene; affected individuals have the sequence GTGGAG. Explain how a researcher would use this information to screen individuals for sickle cell anemia. Clearly describe all the necessary steps beginning with cells from affected and unaffected individuals.

### ***Ethical Issues***

So, SNPs sound useful. Why are SNPs an ethical issue? As with most things, along with the advantages of our increased knowledge of SNPs and the genome come certain risks. There are privacy issues with genetic information, just as there are with medical records. While the information collected by private databases like 23andMe are not publicly available, much of the information about SNPs comes from research that is government funded. Data from these studies are deposited in public databases on the internet that provide open access not only for scientists, but to anyone who searches. Unrelated people differ in about 0.01% of their 3.2 billion nucleotides. Even though there are roughly six billion people on the planet, one single individual can be uniquely identified by only 30 to 80 independent SNP positions. Individuals participating in a research study, for example, may have their SNP profiles posted online. Routine blood samples taken during physical exams could also provide DNA for SNP analysis. Inadvertently, an individual's complete SNP profile could be determined, and the potential risk is that this information may be used or shared in a way unintended by the individual.

The easy availability of data from an individual's genome, including SNPs, raises concerns about the possibility of discrimination, stigmatization, loss of insurance, and loss of employment for the individual and their family members. In a study published in 1999 by Dorothy Wertz, over 1000 U.S. genetics professionals surveyed reported that almost 700 patients had reportedly lost their jobs or insurance because of genetic test results even though they had no symptoms (*Nature Reviews Genetics* 3, 496 (2002); doi:10.1038/nrg854). Terri Seargent's story is not unique.

Lobbyists for the American Council of Life Insurance have argued that if an individual is known to carry genes linked to an increased risk of cancer, the information should be made available when underwriting insurance policies. One possible result is that high-risk individuals may be denied coverage or made to pay higher premiums. Fear of just such an outcome may prevent some individuals from agreeing to testing in the first place. Yet with appropriate genetic test results, physicians are able to monitor high-risk individuals early and regularly for signs of cancer or other treatable diseases. If patients are afraid to be tested, their treatment may be less than optimal. In addition, many individuals are fearful of participating in research projects because they are uncertain of how their genetic privacy will be protected.

Because knowledge of an individual's genetic information could lead to discrimination in hiring practices or rejection of insurance policies, lobbyists from national organizations, such as the National Breast Cancer Coalition and the Council for Responsible Genetics, along with scientists and physicians pushed for laws that protect an individual's genetic information. They wanted a specific law to prevent employers from requiring and using DNA testing in the hiring or firing of employees, to prevent health insurers from requesting or requiring genetic information or using it to determine coverage or rates, and to reassure research participants that their genetic information would remain private. The Genetic Information Nondiscrimination Act, also known as GINA, was first introduced in 1995, and was repeatedly reintroduced without being passed for more than a decade. Critics of the legislation argued that laws already existed that dealt with privacy and genetic information including the American with Disabilities Act (ADA) and the HIPAA privacy act (Health Insurance Portability and Accountability Act of 1996). Both the House and the Senate passed the bill, and former President Bush signed the Genetic Information Nondiscrimination Act into law May 21, 2008. Some have referred to this law as the first civil rights legislation passed in the 21<sup>st</sup> century. The Department of Health and Human Services, along with other federal agencies, will be responsible for enforcing the law.

To understand this case we need to know about the law and about what it does and does not do: Who is protected by the Genetic Information Nondiscrimination Act? Should genetic information be private and protected? Should it be extended to include life, disability, and long-term-care insurance? Why are the members of the military not protected?

*\*\*\* Note: In the time since GINA was signed into law, the Affordable Care Act (ACA) passed. These are two distinct pieces of legislation; although they have some overlap, each provides different protection for the health care consumer. As the following excerpt explains, "GINA is a civil rights statute and has as its purpose the prohibition of discrimination against individuals on the basis of genetic information... GINA not only contains certain requirements for health insurance and a general prohibition of employment discrimination provisions, but also has strong privacy protections. On the other hand, the ACA is comprehensive health care legislation that is intended to, among other things, enhance consumer protections in the private health insurance market and expand health coverage. The ACA, the more recent statute, does not specifically amend GINA and also does not reference GINA's requirements." (Sarata, et al. 2012. The Genetic Information Nondiscrimination Act of 2008 and the Patient Protection and Affordable Care Act of 2010: Overview and Legal Analysis of Potential Interactions. Congressional Research Services).\*\*\**

## ***Your Role***

As the law is currently written, members of the military are excluded. In addition, only health insurance is



covered; GINA does not extend to life, disability or long-term-care insurers. The class will be divided into the lobbying groups listed below. Each lobbying group will work together throughout the case study. Use the online resources provided below to research your position. Each group will discuss the Genetic Information Nondiscrimination Act and related issues, and then organize and present the key arguments from your lobbying group's position to the mock House Subcommittee. *The Subcommittee will be voting on whether or not to amend the law to include protection for individuals in the military and to prohibit life, disability, or long-term-care insurers from using a person's genetic information in determining eligibility or premiums.*

### ***Lobbying Groups***

- Life insurance companies
- Disability & long-term care insurance companies
- National Breast Cancer Coalition
- Genetic counselors
- Physicians
- Advocates for individuals in military
- Companies that design & market genetic tests
- Department of Defense
- Scientists who work on genome research

### ***Links to Websites***

Note that some of the articles posted below require a subscription. If you log on to the Carleton network or to the library web page you will have free access to the articles below.

*SNP background:*

"Making SNPs Make Sense" from Learn.Genetics Genetic Science Learning Center, University of Utah <http://learn.genetics.utah.edu/content/precision/snips/>

"Decodeing Iceland's DNA" from *The Science Creative Quarterly*, August 2003 (SNP profiles are being created for the entire population) <http://www.bioteach.ubc.ca/Bioinformatics/DeCODE/>

*Background on Genetic Information Nondiscrimination Act:*

Summary:

<http://www.hhs.gov/ohrp/policy/gina.html>

<http://www.genome.gov/10002328>

<https://www.genome.gov/10002077/genetic-discrimination/>

[https://www.eeoc.gov/laws/regulations/gina\\_qanda\\_smallbus.cfm](https://www.eeoc.gov/laws/regulations/gina_qanda_smallbus.cfm)

"Keeping Pace with the Times--The Genetic Information Nondiscrimination Act of 2008" Editorial from *New England Journal of Medicine*, 2008 <http://www.nejm.org/doi/full/10.1056/NEJMp0803964>

"The Loopholes in the Law Prohibiting Genetic Discrimination" from *The Atlantic*, March 2017 <https://www.theatlantic.com/health/archive/2017/03/genetic-discrimination-law-gina/519216/>

"GINA and Employee Wellness Programs" from National Institutes of Health's National Human Genome Research Institute <https://www.genome.gov/27568501/gina-and-employee-wellness/gina-and-employee-wellness/>

Examples of GINA lawsuits:

<http://www.eeoc.gov/eeoc/newsroom/release/1-13-14.cfm>

<https://www.eeoc.gov/eeoc/newsroom/release/6-23-16.cfm>

*Military and genetic information:*

“Civilian and Military Genetics: Nondiscrimination Policy in a Post-GINA World” from *American Journal of Human Genetics*, October 2008 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2561935/>

“Pulling rank: Why should US military personnel be singled out for genetic discrimination?” from *Nature*, August 2007 <http://www.nature.com/nature/journal/v448/n7157/full/448969a.html>

“Genomic medicine in the military” from *Genomic Medicine*, January 2016 <https://www.nature.com/articles/npjgenmed20158>

“Challenges for implementing a PTSD preventative genome sequencing program in the U.S. military” from *Case Western Reserve Journal of International Law*, 2015 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4577019/>

*Personal genomes and genetic testing:*

Genetic Testing background  
<http://www.nlm.nih.gov/medlineplus/genetictesting.html>

“Can Anyone Make Sense -- or Money -- Out of Personal DNA Testing?” from Knowledge@Wharton, June 2007 <http://knowledge.wharton.upenn.edu/article.cfm?articleid=1757>

“Getting Up Close and Personal with Your Genome” from *Cell*, May 2008  
<http://www.sciencedirect.com/science/article/pii/S0092867408006235>

“Googling the genome” editorial by Glyn Moody from *The Guardian*, April 2004  
<http://www.guardian.co.uk/technology/2004/apr/15/genetics.science>

“Pharmacogenetics to come” from *Nature*  
<http://www.nature.com/nature/journal/v425/n6960/full/425749a.html>

23andMe <https://www.23andme.com/>

AncestryDNA <https://www.ancestry.com/dna/>

*Genetics, Medicine, and Insurance:*

“Do not ask or do not answer?” from *The Economist* August 2007  
[http://www.economist.com/science/displaystory.cfm?story\\_id=9679893](http://www.economist.com/science/displaystory.cfm?story_id=9679893)

“Personal genomics and the end of insurance” from *Venture Beat* September 2007  
<http://venturebeat.com/2007/09/11/personal-genomics-and-the-end-of-insurance/>

“Bridging the gap between life insurer and consumer in the genetic testing era: The RF proposal” from *Indiana Law Journal*, 1999 <http://www.repository.law.indiana.edu/ilj/vol74/iss4/8/>

“The genetic information nondiscrimination act — a half-step toward risk sharing” from *The New England Journal of Medicine*, 2008 <http://www.nejm.org/doi/full/10.1056/NEJMp0804352>

“Pink Slip in your Genes” from *Scientific American*, 2001 <http://www.mult-sclerosis.org/news/Jan2001/GeneticDiscrimination.html>



“Ethical Issues of Predictive Genetic Testing for Diabetes” from *Journal of Diabetes Science and Technology*, 2009 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2769962/>

“Factors associated with experiences of genetic discrimination among individuals at risk for Huntington disease” from *The American Journal of Medical Genetics*, 2013 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3860279/>

“Genetic information, non-discrimination, and privacy protections in genetic counseling practice” from *Journal of Genetic Counseling*, 2014 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4233176/>

“Confidentiality & the risk of genetic discrimination: What surgeons need to know” from *Surgical Oncology Clinics* October 2015 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4568442/>

“If you want life insurance, think twice before getting a genetic test” from *Fast Company*, February 2016 <https://www.fastcompany.com/3055710/if-you-want-life-insurance-think-twice-before-getting-genetic-testing>

“The flip side of personal genomics: When a mutation doesn’t spell disease” from *Nature*, November 2016 <https://www.nature.com/news/the-flip-side-of-personal-genomics-when-a-mutation-doesn-t-spell-disease-1.20986>

“Sophia Genetics raises \$30 million to help doctors diagnose using AI and genomic data” from *Venture Beat* September 2017 <https://venturebeat.com/2017/09/13/sophia-genetics-raises-30-million-to-help-doctors-diagnose-using-ai-and-genomic-data-analysis/>

“New Gene Tests Pose a Threat to Insurers” from *The New York Times*, May 2017 <https://www.nytimes.com/2017/05/12/health/new-gene-tests-pose-a-threat-to-insurers.html>

“Genetic testing threatens the insurance industry” from *The Economist*, August 2017 <https://www.economist.com/news/finance-and-economics/21725783-insurers-worry-about-adverse-selection-insured-worry-about>

#### *Research subject privacy:*

“Genomic research and human subject privacy” from *Science*, July 2004 <http://science.sciencemag.org/content/305/5681/183>

“Toward protecting participants’ privacy” from *The Scientist*, October 2015 <http://www.the-scientist.com/?articles.view/articleNo/44369/title/Toward-Protecting-Participants--Privacy/>

“DNA scan for infants raise questions of privacy and discrimination,” from CBS News, October 2017 <https://www.cbsnews.com/news/dna-scan-for-infants-disease-privacy-discrimination/>

“Public Opinion about the Importance of Privacy in Biobank Research” from *American Journal of Human Genetics*, 2009 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2775831/>

#### *Advocacy Groups:*

National Breast Cancer Coalition: <http://www.breastcancerdeadline2020.org/breast-cancer-information/>

American Benefits Council: <http://www.americanbenefitscouncil.org/>

American Benefits Council, Health Non-Discrimination Issues (including re: GINA):  
<https://www.americanbenefitscouncil.org/our-issues/health/non-discrimination-issues/>

Veterans and military families for progress: <http://www.vmfp.org/>

*Legislation related to GINA:*

Health Insurance Portability and Accountability Act  
<http://www.hhs.gov/ocr/hipaa/>

ADA  
<http://www.ada.gov>

Image Credit: Drawing of chromosome to base pairs provided courtesy of The U.S. Department of Energy (DOE), the DOE Joint Genome Institute (JGI), and the Lawrence Berkeley National Laboratory (LBNL) Creative Services Office.

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