A Single Nucleotide Polymorphism, or SNP ("snip"), is a small genetic change, or variation, that can occur within a person's DNA sequence. An example of a SNP is the alteration of the DNA segment AAGGTTA to ATGGTTA, where the second "A" in the first snippet is replaced with a "T". On average, SNPs occur in the human population more than 1 percent of the time. Because only about 3 to 5 percent of a person's DNA sequence codes for the production of proteins, most SNPs are found outside of coding sequences. SNPs found within a coding sequence are of particular interest to researchers because they are more likely to alter the biological function of a protein.

Many diseases in humans are not caused by a genetic variation within a single gene but are influenced by complex interactions among multiple genes as well as environmental and lifestyle. Although both factors add tremendously to the uncertainty of developing a disease, it is currently difficult to measure and evaluate their overall effect on a disease process. Therefore, we refer here mainly to a person's genetic predisposition, or the potential of an individual to develop a disease based on genes and hereditary factors. Genetic factors may confer susceptibility or resistance to a disease and determine the severity or progression of disease. Because we do not know all of the factors involved in these pathways, researchers have found it difficult to develop screening tests for most diseases and disorders. By studying stretches of DNA that have been found to harbor a SNP associated with a disease trait, researchers may begin to reveal genes associated with a disease. Defining and understanding the role of genetic factors in disease will also allow researchers to better evaluate the role non-genetic factors—behavior, diet, lifestyle, and physical activity—have on disease. Because genetic factors also affect a person's response to drug therapy, DNA polymorphisms such as SNPs will be useful in determining and understanding why individuals differ in their abilities to absorb or clear certain drugs, as well as to determine why an individual may experience an adverse side effect to a particular drug. Therefore, the recent discovery of SNPs promises to revolutionize not only the process of disease detection but the practice of preventative and curative medicine.

SNPs and Disease Diagnosis Each person's genetic material contains a unique SNP pattern that is made up of many different genetic variations. Researchers have found that most SNPs are not responsible for a disease state. Instead, they serve as biological markers for pinpointing a disease on the human genome map, because they are usually located near a gene found to be associated with a certain disease. Occasionally, a SNP may cause a disease and, therefore, can be used to search for and isolate the disease-causing gene (ex. sickle cell disease). To create a genetic test that will screen for a disease in which the disease-causing gene has already been identified, scientists collect blood from a group of individuals affected by the disease and analyze their DNA for SNP patterns. Next, researchers compare these patterns to patterns obtained by analyzing the DNA from a group of individuals unaffected by the disease. This type of comparison, an "association study", can detect differences between the SNP patterns of the two groups, indicating which pattern is most likely associated with the disease-causing gene. SNP profiles that are characteristic of a variety of diseases will be established. Then, it will be a matter of time before physicians screen individuals for susceptibility to a disease by analyzing DNA samples for SNP patterns.

SNPs and Drug Development SNPs may also be associated with the absorbance and clearance of therapeutic agents. Currently, there is no simple way to determine how a patient will respond to a particular medication. A treatment proven effective in one patient may be ineffective in others. Worse yet, some patients may experience an adverse immunologic reaction to a particular drug. Today, pharmaceutical companies are limited to developing agents to which the "average" patient will respond. As a result, many drugs that might benefit a small number of patients never make it to market. In the future, the most appropriate drug for an individual could be determined in advance of treatment by analyzing a patient's SNP profile. The ability to target a drug to those individuals most likely to benefit, referred to as "personalized medicine", would allow pharmaceutical companies to bring more drugs to market and allow doctors to prescribe individualized therapies specific to a patient's needs.
PHARMACOGENOMICS and SNPs  doegenomes.org  Human Genome Project Information
Pharmacogenomics is the study of how genetic inheritance affects the body's response to drugs. It is the intersection of pharmaceuticals and genetics. Pharmacogenomics holds the promise that drugs might one day be tailor-made for individuals and adapted to each person's own genetic makeup. Environment, diet, age, lifestyle, and state of health all can influence a person's response to medicines, but understanding an individual's genetic makeup is the key to creating personalized drugs with greater efficacy and safety. Pharmacogenomics combines traditional pharmaceutical sciences such as biochemistry with annotated knowledge of genes, proteins, and single nucleotide polymorphisms (SNPs).

What are the anticipated benefits of pharmacogenomics?

- **Powerful Medicines**  Pharmaceutical companies will create drugs based on proteins, enzymes, and RNA molecules associated with genes and diseases to produce a therapy targeted to specific diseases.
- **Better, Safer Drugs the First Time**  Instead of standard trial-and-error method of matching patients with the right drugs, doctors will analyze a patient's genetic profile and prescribe the best available drug therapy from the beginning. Not only will this take guesswork out of finding the right drug, it will speed recovery and increase safety as the likelihood of adverse reactions is eliminated.
  Pharmacogenomics has the potential to reduce the estimated 100,000 deaths and 2 million hospitalizations that occur each year in the United States as the result of adverse drug response.
- **More Accurate Methods of Determining Appropriate Drug Dosages**  Current methods of basing dosages on weight and age will be replaced with dosages based on a person's genetics --how well the body processes the medicine and the time it takes to metabolize it.
- **Advanced Screening for Disease**  Knowing one's genetic code will allow a person to make adequate lifestyle and environmental changes at an early age so as to avoid or lessen the severity of a genetic disease. Likewise, advance knowledge of a particular disease susceptibility will allow careful monitoring, and treatments can be introduced at the most appropriate stage to maximize their therapy.
- **Better Vaccines**  Vaccines made of genetic material promise all the benefits of existing vaccines without the risks. They will activate the immune system but will be unable to cause infections. They will be cheaper, stable, and capable of being engineered to carry several strains of pathogen at once.
- **Decrease in the Overall Cost of Health Care**  Decreases in the number of adverse drug reactions, the number of failed drug trials, the time it takes to get a drug approved, the length of time patients are on medication, the number of medications patients must take to find an effective therapy, the effects of a disease on the body (through early detection), and an increase in the range of possible drug targets will promote a net decrease in the cost of health care.

What are some of the barriers to pharmacogenomics progress?

- **Complexity of finding gene variations that affect drug response** - Single nucleotide polymorphisms (SNPs) are DNA sequence variations that occur when a single nucleotide in the genome sequence is altered. SNPs occur every 100 to 300 bases along the 3-billion-base human genome, therefore millions of SNPs must be identified and analyzed to determine their involvement (if any) in drug response. Further complicating the process is our limited knowledge of which genes are involved with each drug response. Since many genes are likely to influence responses, obtaining the big picture on the impact of gene variations is highly time-consuming and complicated.
- **Drug alternatives** - Only one or two approved drugs may be available for treatment of a condition. If patients have SNPs that prevent them using the drugs, they may be without alternatives for treatment.
- **Disincentives for drug companies to make multiple pharmacogenomic products** - Most pharmaceutical companies have been successful with their “one size fits all” approach to drug development. Since it costs hundreds of millions of dollars to bring a drug to market, will these companies be willing to develop alternative drugs that serve only a small portion of the population?
- **Educating healthcare providers** - Introducing multiple pharmacogenomic products to treat the same condition for different population subsets will complicate the process of prescribing and dispensing drugs. Physicians must execute an extra diagnostic step to determine which drug is best for each patient. To interpret the diagnostic accurately and recommend the best course of treatment for each patient, all prescribing physicians, regardless of specialty, will need a better understanding of genetics.