Mutation or polymorphism?

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DNA sequence variations are sometimes described as mutations and sometimes as polymorphisms. What is the difference between these terms and how are they applied to the human genome?

A **mutation** is defined as any change in a DNA sequence away from normal. This implies there is a normal allele that is prevalent in the population and that the mutation changes this to a rare and abnormal variant.

In contrast, a **polymorphism** is a DNA sequence variation that is common in the population. In this case no single allele is regarded as the standard sequence. Instead there are two or more equally acceptable alternatives. The arbitrary cut-off point between a mutation and a polymorphism is 1 per cent. That is, to be classed as a polymorphism, the least common allele must have a frequency of 1per cent or more in the population. If the frequency is lower that this, the allele is regarded as a mutation.

Why are some sequence variants more common than others? Sequence variants that directly and overtly cause human diseases are generally rare in the population because they reduce fitness. Such disease alleles are classed as mutations. However, not all mutations cause diseases. Any new sequence variant, even if neutral or beneficial in effect, will start off as a rare mutation.

Polymorphic sequence variants usually do not cause overt debilitating diseases. Many are found outside of genes and are completely neutral in effect. ***Others may be found within genes, but may influence characteristics such as height and hair colour rather than characteristics of medical importance.*** However, polymorphic sequence variation does contribute to disease susceptibility and can also influence drug responses (Single Nucleotide Polymorphisms). SNPs occur about once every 1000 base pairs in the genome, making up the bulk of the 3 million variations found in the genome. Unlike the other, rarer kinds of variations, many SNPs occur in genes and in the surrounding regions of the genome that control their expression. The effect of a single SNP on a gene may not be large - perhaps influencing the activity of the encoded protein in a subtle way - but even subtle effects can influence susceptibility to common diseases, such as heart disease or Alzheimer's disease.

The above definitions cannot be applied rigorously***. A rare disease allele in one population can become a polymorphism in another if it confers an advantage and increases in frequency.*** A good example is the allele of sickle-cell disease. In Caucasian populations this is a rare sequence variant of the beta-globin gene that causes a severely debilitating blood disorder. In certain parts of Africa, however, the same allele is polymorphic because it confers resistance to the blood-borne parasite that causes malaria.

http://genome.wellcome.ac.uk/doc_WTD020780.html