'Genotype vs Phenotype' Brittany C. Burns MD

The **genotype** is the genetic makeup of an individual. It is a map for all our proteins that build our organs, tissues, hormones, receptors, neurotransmitters, etc. There are two alleles for any given gene. You inherit one allele from each parent via random selection. Dominant alleles will guarantee inheritance of that trait, while recessive alleles can remain hidden until 2 alleles are inherited together to display the trait. An example of this is the human CFTR gene, which encodes a protein that transports chloride ions across cell membranes, can be dominant (A) as the normal version of the gene, or recessive (a) as a mutated version of the gene. Individuals receiving two recessive alleles will be diagnosed with the disease of Cystic Fibrosis.

Genetic mutations that appear to predispose illness in certain situations can also have once provided protection in certain environments. A good example of this is with Sickle Cell disease. Carriers of the recessive sickle cell trait have a natural protection against malaria, however the unfortunate individual who receive 2 alleles of sickle cell trait will demonstrate the debilitating disease of sickle cell. In the environment where malaria was more lethal than the 25% born with sickle cell disease, it provided the people who inherited this trait an advantage and thus multiplied. Now this trait, in our current environment, only conveys disease. Both your inherited genotype and non-hereditary environmental variation contribute to the **phenotype** of an individual. The **phenotype** is how you display your genetic potential. This concept is most impressively demonstrated with identical twins that have been separated early in life, and ultimately display very different **phenotypes** despite their identical **genotypes**. We all have the potential for disease, some more so than others depending on your **genotype**. It is important to realize that most disease is not hardwired like the examples of sickle cell or cystic fibrosis above, but rather confer a predisposition that may or may not be expressed depending on life exposures.

Many genes that may now predispose disease once conveyed a protective element in certain settings. This phenomenon can be applied to much of illness and novel adaptation, however, often in subtle variances. We see clustering of genetic variance depending on peoples heritage, such as Cystic fibrosis trait is more prevalent in Caucasians with European decent and Sickle Cell in African Americans from certain regions in Africa with high prevalence of Malaria. Likewise, we see people of certain heritage with increased prevalence and predisposition to Obesity and Diabetes. There is this idea of the "thrifty gene hypothesis", where people of more recent 'hunter and gatherer' background carry a genetic makeup that once allowed them to hold and store calories during times of feast so that they survive and thrive more readily during times of famine. Now, in this age where food is readily available 24/7 and does not require energy expenditure to acquire, these same genes predispose Obesity and the expression of disease in the form of Diabetes.

We see this genetic portfolio predisposing obesity and diabetes prevalent among, for instance, the Native Americans and Samoan people. Their genetics do not guarantee manifestation of disease, but rather predispose disease in our current environment with sedentary lifestyles and diet rich in carbohydrates such as grains and sugar. An individual with this predisposition must work in some ways harder to maintain healthy body weights to avoid the vicious cycle of hyperinsulinemia, weight gain, and insulin resistance that leads to type 2 Diabetes. These same people tend to thrive on the Paleo diet that is far lower in refined grains, sugars, and simple carbohydrates, which their Ancestors were not accustomed nor exposed to.

Agriculture - including the growing of grain crops, like wheat and barley, has only been practiced for around ten thousand years, a relatively short time compared to how long humans have been eating other foods (e.g. digestion-friendly meat, fish, vegetables and fruits) - 2.5 million years. Our bodies have not

evolved as fast as our ability to produce Modern Foods. In fact our capacity to grow grain crops like wheat, corn and rye has far outstripped our digestive systems' development. That is, we do not yet have all the necessary biological equipment to process these proteins (gluten) effectively without consequences of varying degrees of inflammation in most and disease in many. Inflammation, remember, is the ignition or fuel of most disease and illness. Without inflammation, cholesterol does not stick and form plaque in our arteries predisposing to stroke and heart disease. Without inflammation, our immune system is less inclined to turn on itself and exhibit autoimmune disease. Without inflammation, cancer is much less prevalent. Inflammation ages us and ails us. While we cannot avoid all inflammation, like stress in our lives, we frequently do have power and choice over much of our practices that contribute to inflammation.

Much of western illness is fuelled not only by inflammation but also sedentary lifestyle, and hormonal imbalance. Hormones are held in delicate balance and are influenced intimately by our lifestyles—by diet, stress, activity level, weight, and sleep. Our diets in turn influence our weight, cholesterol, inflammation, and hormonal balance. These factors are all intertwined and imposing to varying degrees depending on our genetic foundation. Some individuals may have to work very hard to increase their metabolic rate and maintain healthy body weight, while other run hot and have troubles keeping the weight on. Much of this is driven by your genetic make-up, but it does not mean that you cannot achieve a healthy body weight; it just means you may have to work harder and be more vigilant to achieve it!

Both your inherited **genotype** and non-hereditary environmental variation contribute to your **phenotype** or how you express your genetic potential. While we cannot control the genes we are dealt, we can to some degree control how they are expressed by the choices we are able to make in our lifestyle. It is true that are bodies are amazing and adaptive and can utilize a wide variety of fuels, but it is also true that there are superior fuels that humans are more adapted to utilize more cleanly without the byproducts of disease that accumulate over time. In the past Natural Selection would sift out those who demonstrated disease that in turn made them less fit in their given environment. Current medical aid and social subsidies may be argued to blunt the affects of Natural Selection, thus carrying forward genes that predispose disease. We must therefore, learn to manipulate our environments so that we do not express these diseases and we can learn to do so by building knowledge of what promotes disease processes.

We cannot expect our genotype to adapt over our lifetime. We still must try to live true to the fuels that our bodies are most adept at processing cleanly. This remains to be: adequate sleep, routine exercise, play, a wholesome low inflammatory diet, avoiding smoking and excess alcohol, and minimizing life stressors. Make sure to keep vigor in your life with exercise, play, and healthy relations, as these factors are the most potent influences in my experience to success of longevity with grace and quality. Remember, it is not only about living a long life, it is more importantly about the quality of life and maintaining independence of mind and body into your later years. We all are dealt a hand from a genetic "deck of cards"- how you play that hand is up to you! I encourage you all to empower yourself with knowledge and to be insightful on health and habits that may help you live longer healthier lives with the genes you've got!