Personalized
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# PERSONALIZED HEALTH AND GENETIC TESTING

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Ponce de Leon's legendary search for the Fountain of Youth exemplifies the human desire for a long and healthy life. The innate, even desperate, belief in an elixir with magical rejuvenative powers demonstrates how mysterious and sometimes elusive health can seem to be.

As a result of the human genome project and subsequent research involving genetics, scientists have been able to unravel many of the mysteries surrounding health, disease and longevity. It is now possible to search within our DNA for glitches that could result in disease given certain environmental conditions.

As scientists learn more, access to details about our genetic make-up are becoming increasingly available. Labs that offer direct-to-consumer analysis have appeared on the scene. Healthcare providers have discovered the power of genetic testing as a diagnostic tool, one that can illuminate the underlying cause of a mysterious illness or previously unknown factor involved in a disease.

As thrilling as it could be to dig into genetic secrets that might predict the future, it could also be unnerving to learn of a latent illness in oneself or one's offspring. This paper is intended to help consumers intelligently address the genetic testing option by highlighting a few specifics about the science of genetics and the potential benefits of learning about our personal genetic code.

## The Basics of Genetics

We are a unique combination of genetic traits inherited from our parents. At fertilization, 23 chromosomes from a father are joined to 23 chromosomes from a mother to form the 23 pairs for each cell of the new life created. Identical chromosome pairs reside in the nucleus of every cell and are composed of single, long DNA molecules (deoxyribonucleic acid) that are spiral-shaped, like twisted ladders hooked together at the "rungs" by nucleotide pairs. A group of nucleotides function together as genes, which are essentially codes for the body to manufacture proteins. These proteins then perform important biochemical functions.

Matching genes on each pair of chromosomes, called alleles, can express the same trait (homozygous) or different traits (heterozygous). Some genes are dominant and will be expressed in homozygous and heterozygous combinations. Recessive genes will only be

expressed if they are homozygous, in other words, if the same recessive trait is inherited from both parents. Interestingly, one or both parents may carry these genes with no physical expression of the genes in themselves. Recessive inheritance can result in remarkable physical traits like green eye color or attached ear lobes. Less benign recessive inheritances can also occur including cystic fibrosis and Phenylketonuria (PKU) (1).

It may be hard to imagine, but gender is determined by only one pair of the 23 pairs of chromosomes. The father passes on either an X chromosome or a Y chromosome to the child. The mother passes on one or the other of her two X chromosomes. When the parent's chromosomes pair together, the child's gender is determined. Two X chromosomes will produce a female child and one of each, X and Y, will produce a male child. It is interesting to note that the X chromosome contains 800 to 900 genes and the Y chromosome is much smaller with only 50 to 60 genes (2). Obviously, not all of the genes on the X chromosome have corresponding alleles, which is why a boy can more easily inherit recessive traits from his mother (3).

One's particular arrangement of genes is his genotype. When a gene is expressed, the resulting traits are collectively known as the phenotype. Since not all genes are expressed, even identical twins can display different traits though they start out with the same genotype. Variations among siblings typically result from the pairings of dominant and recessive genes, which differ from child to child as a result of chromosomal gene swapping in the parent's gametes prior to fertilization for each child (4).

## Epigenetics

Not all variations in gene expression result from the genotype. Other factors are involved. Barring mutation, the genotype remains constant as cells divide after fertilization of the gametes. Each new cell contains the exact genetic code of the previous cells as they divide. Modifications to the organism occur with the help of other molecules that turn on or turn off certain genes on the strands of DNA, controlling the progression to produce different cell types that eventually form nerves, muscles, bones, organs, and so on, that all work in concert with one another. We inherit some of these modifiers from our parents, but not all modifiers are passed along (5).

Modifications continue to occur to our genes throughout our lives as part of our adaptation to an ever-changing environment (6). The study of these modifications is known as epigenetics ((Epi = above, Epigenetic= above genetic). Epigenetics refers to any process that alters gene expression without changing the genotype and is heritable by the daughter cells (7). These alterations are accomplished through a variety of mechanisms including chemical changes in the microscopic environment and the influence of certain proteins that regulate gene expression (8).

The exciting news is that genes alone do not determine our destiny! The discovery of epigenetics has opened up new possibilities for disease prevention and treatments. In many instances what drives epigenetic variations are factors that we can control. What if we could have a health plan personally tailored based on what our genes are telling us we need?

Certain of these controllable factors seem obvious: avoiding cigarette smoke and other pollutants as much as possible; eating a plant-based diet rich in phytonutrients, vitamins and minerals; eating healthy proteins and fats; drinking pure water throughout the day; exercising on a daily basis and avoiding overeating. Less obvious factors may involve behavior: meditating daily; physical contact with loved-ones; enjoyment of music; thinking positive thoughts; and finding reasons to laugh (9).

In conjunction with expert nutritional advice, the implications of genetic testing extend from the macroscopic: which exercise regimen is the most beneficial for an individual's muscle type and unique biochemical functions; to the microscopic: what form of a vitamin is best for his or her specific biochemistry; which biochemical pathway is being under-utilized; and what nutrients may be needed in higher or lower amounts. The possibilities are nearly endless.

Perhaps, the resolution to Ponce de Leon's dilemma rests in the influence we have over our own epigenetic expression and how we allow our genes to interact with the environment.

## What Genetic Testing Tells Us

Our modern understanding of epigenetics has created an exciting new field that is, in large part, the drive behind individual genetic testing. Genetic testing, however, doesn't actually measure epigenetic modifiers but, instead, measures mutations or Single Nucleotide Polymorphisms (SNPs) within the genetic code. SNPs occur on the building blocks of DNA where the rungs of the ladder are bonded together.

There are only four possible nucleotides located on a chromosome's rungs: adenine (A), cytosine (C), guanine (G) and thymine (T). Their arrangement on the DNA molecule determines which proteins will be coded by them.

Each nucleotide on a chromosome is matched to specific nucleotide on the opposite DNA molecule of the spiral. Adenine always pairs with thymine, for example, and cytosine always pairs with guanine. When one nucleotide is swapped for another, this is known as a SNP. These polymorphisms can cause a malformed protein or enzyme to be coded by the DNA. Since enzymes facilitate specific chemical reactions in our cells, if even one type of enzyme is malformed, then important processes in the body could be impaired. The severity will depend on whether or not the SNP occurs on only one of the chromosomes in the pair that carries that gene (heterozygous) or both of chromosomes that carry that gene (homozygous) (10).

SNPs arise fairly frequently, about one in every 300 nucleotides, and are a normal aspect of genetic variation. While many nucleotides are not actually part of the gene portion of the DNA

strand, and have little or no effect on the phenotype, others occur where DNA regulates genes or on the genes themselves. The expression of these genes then depends on epigenetic influences.

To illustrate what genetic testing can offer to us and how a skilled clinician can advise us on optimizing our health, let's look more into the relatively common MTHFR polymorphism.

The MTHFR gene codes for the enzyme of the same name, methylenetetrahydrofolate reductase. The MTHFR polymorphism occurs when a single nucleotide, cytosine, is replaced with the nucleotide, thymine, at position 677 on the gene (11). The enzyme, MTHFR, converts the B-vitamin, folate, to a chemical form necessary for performing important functions in the body including the conversion of homocysteine to methionine and the formation of the endogenous antioxidant, glutathione. If these chemical reactions are compromised by the polymorphism, then a person could have increased chances of developing cardiovascular disease and have impaired detoxification function in the liver (12).

It may seem daunting that such a small change can create disease. The good news is that a skilled clinician, one who takes your personal genetic variation into account, can tailor nutritional advice specific to your nutritional, even genetic, requirements, and treat or possibly prevent disease (13).

## Prevention and Targeted Treatment – The New Paradigm

The advice that a doctor or nutritionist gives to a patient need no longer take the form of a blanket statement like, "eat your vegetables!" It can instead be tailored to the specific needs of each individual. One person may be told that she needs more raw leafy green vegetables due to the MTHFR polymorphism and another person may be told to eat more tomatoes for the lycopene to help prevent macular degeneration (14)(15).

The future of cancer prevention and treatment is also promising. New studies are being conducted and published showing that specific nutrients and drugs are found to reverse cancer progression. One 2005 study concerning colorectal adenoma associated with a genetically induced folate deficiency, for example, showed significantly improved outcomes with folic acid supplementation (16).

On the horizon, investigation has begun into cancer treating drugs that target aberrant patterns in gene regulation (polymorphisms) that are associated with specific cancers. (17) The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins is currently performing clinical trials using such epigenetic treatments. (18)

## How to Get Tested

Many of the labs that offer genetic testing provide databases that list clinicians who utilize their services. If you are not already under the guidance of a healthcare provider who has suggested testing and you need to locate one, this may be a good place to begin your search. Many of the labs also provide nutritional and genetic counseling.

Even as reliable tests for genetic predisposition become increasingly available, a professional who understands the tests, can interpret the information, and has the experience to provide sound advice based on that information, is an integral component in any successful outcome. A healthcare provider who understands your family health history and your personal health needs, can also help you find the most cost effective tests to order.

## Glossary of Terms

**Allele**
One of two versions of a gene that occupy identical positions on a chromosome pair.

**Amino acid**
One of 20 organic molecules that bond to one another in various sequences to form proteins. Construction of the proteins is under the control of DNA.

**Chromosome**
A single molecule of DNA and associated proteins that carries heritable genetic information. Chromosomes are found in the nuclei of cells. Humans have 22 pairs of matched chromosomes (autosomes) plus one pair of sex chromosomes, X and Y, that differ in length.

**Colorectal adenoma**
A benign tumor in the lining of the colon and/or rectum that commonly appears as a polyp during a colonoscopy. Untreated adenoma can progress to malignant adenocarcinoma.

**Crossing over**
The process by which genetic information passes between paired strands of DNA during meiotic cell division.

**Cystic fibrosis**
An inherited disease affecting the exocrine glands typified by chronic respiratory issues including mucus build-up in the lungs and resulting respiratory infection. Cystic Fibrosis is carried as a recessive trait on a single gene.

**DNA**
Deoxyribonucleic acid: the self-replicating macro-molecule that is the primary constituent of chromosomes.

**Dominant gene**
The form of a gene (allele) that is expressed in a heterozygous pair.

**Enzyme**
A biological catalyst that increases the rate of a specific biochemical reaction.

**Epigenetics**
The study of environmental influences on the expression of genetic information.

**Gene**
The fundamental unit of inheritance. Each gene occupies a specific location on a specific chromosome and generally corresponds to a certain inherited trait in an organism.

**Genome**
The entire set of genetic instructions in an individual's chromosomes including genes and their arrangement. Contrast with phenome – an individual's observable traits.

**Genotype**
Generally, the collection of genes that make up an individual's genome. Can also refer to the details of a specific gene.

**Heterozygous**
A state in which the forms of a specific gene inherited from each parent (alleles) differ. In this state, dominant/recessive interactions come into play.

**Homozygous**
A condition in which the forms of a specific gene inherited from each parent are identical. Even recessive genes will be expressed in this state since they are not masked by a dominant gene.

**Mutation**
A structural deviation in the composition of a gene. Since the majority of mutations occur in unexpressed parts of the chromosome, most produce no observable effect. Those that occur in critical genes can result in expressions ranging from beneficial to disastrous. Mutations are differ from sequencing that is prevalent in the population and is considered an abnormal variant.

**Non-coding DNA**
DNA sequences that do not control the production of proteins. While most non-coding DNA has no known function, there is evidence that it plays a role in regulating gene expression.

**Nucleotide**
The building block of nucleic acids like DNA.

**Phenotype**
An individual's observable traits as contrasted with his genetic make-up.

**PKU**
Phenylketonuria. An inheritable, progressively debilitating disease in which the amino acid, phenylalanine is not properly metabolized. If discovered in time, the effects of PKU can be mitigated by diet.

**Recessive gene**
The form of a gene (allele) that is suppressed (masked) in a heterozygous pair.

**Single Nucleotide Polymorphism (SNP)**

A gene variation that occurs due to a substitution of one nucleotide for another. They occur in

about 1 in every 1,000 within the code and usually produce no observable effects. Their occurrences are more common than mutations and do not usually produce overt disease characteristics. Some, however can increase susceptibility to disease, as well as, influence drug response.

For more details on these terms and to learn more, visit The National Human Genome Research Institute's website at: http://www.genome.gov/glossary/index.cfm

| Lab | url | Direct to Consumer | Counseling Available | Types of Tests | | | | DNA & SNPs Tested for: | Multiple SNPs? | Turn Around Time |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | SNP | Drug Metabolism | Ancestry | Detailed Report | | | |
| **DNATraits** | https://www.dnatraits.com/default.aspx | No | No | | No | No | unknown | BRAC1 & BRCA2 | unknown | unknown |
| **The Genetic Testing Laboratories, Inc. (GTL)** | http://www.gtldna.com/ | Yes | Yes | Yes | No | Yes, but done separately | Yes | Multiple Disease predispositions | Multiple Locations Tested | 5 Days |
| **Pathway Genomics** | https://www.pathway.com/ | Pathway Fit can be order directly The other test require a healthcare professional | Yes | Yes | Yes | No | Yes | Fitness Profile Cancer Risk Profile Cardiac Profile Weight -Management Genetic Disease: In-born Errors of Metabolism, Mental Health Pain Medication Metabolism | Multiple Locations Tested | Varies |
| **23andMe** | https://www.23andme.com/ | yes | No | Yes | No | Yes | No, Requires Genetic Genie to interpret profile: http://geneticgenie.org/ | Ancestry information is given. At this time raw genetic data is given without interpretation pending FDA authorization. | Methylation and Detox Profiles | 6 to 8 weeks |
| **Gene Planet** | http://www.geneplanet.com/ | Yes. This is a European Company | Yes | Yes | Yes | No | Yes | Multiple Disease Predisposition, Drug Metabolism, Traits, Fitness Profile | Multiple locations Tested | 40 days |
| **Genova** | http://www.gdx.net | No | Expected to be done through healthcare provider | Yes | Yes | No | Yes | Cardio profile Detox profile – includes drug metabolism, methylation Immune Response Estrogen | Multiple Locations Tested | 21 days |

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|---|---|---|---|---|---|---|---|---|---|---|
| **SpectraCell Laboratories** | http://www.spectracell.com/clinicians/products/ | No | Expected to be done through healthcare provider | Yes | No | No | Basic | Telomere Score<br>APOE Genotype<br>MTHFR<br>C677T and A1298C | Multiple SNPs for APOE, 2 SNPs are tested for MTHFR | 7 to 10 days |
| **Ambry Genetics** | http://www.ambrygen.com/ | No | Yes | Mutations and SNPs | Yes | No | Report is given to healthcare provider | Cancer risk<br>Cardio profile<br>Autism Spectrum Disorder<br>BRCA1, BRCA2 and many diseases | Tests for mutations and SNPs | 10 days to 16 weeks depending on tests ordered |
| **Myriad** | https://www.myriad.com/physicians/genetic-testing/ | No | Expected to be done through healthcare provider | Mutations | Tests for chemo-toxicity for cancer treatment | No | Report is given to healthcare provider | Cancer Risk for Breast, Ovarian, Uterine, Melanoma, Pancreatic and Prostate | Tests for mutations | Two weeks or longer |
| **Athena** | http://www.athenadiagnostics.com/content/index.jsp | No | Expected to be done through healthcare provider | Mutations and SNP | Yes | No | Report is given to healthcare provider | DNA Sequencing, 509 diseases, specialize in neurology, endocrinology and nephrology | Tests for mutations Multiple sites tested | varies |
| **Correlagen (LabCorp)** | https://www.correlagen.com/index.jsp | No | Expected to be done through healthcare provider | Mutations and SNPs | No | No | Report is given to healthcare provider | DNA Sequencing, Endocrine, Cardiac, Autoimmunity, and other diseases | Tests for mutations and SNPs | Claims to be short on website |

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## About the Authors

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Brenda Dyson is a holistic health practitioner combining advanced bodywork, fitness education and nutritional consultation. She has over 20 years of experience as a massage therapist, Rolfer®, and craniosacral therapist, as well as a Master's Degree in Human Nutrition from the University of Bridgeport and a Bachelor's Degree in Physical Education from Towson University in Baltimore, Maryland. She taught Life Fitness and Wellness classes at the Community College level in Maryland for 10 years. She currently lives in sunny St. Augustine, Florida where she loves to run, bike, tend to her garden and practice yoga.

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Dr. Minich has a unique approach to clinical medicine based in a combination of physiology and psychology. She has trained in functional medicine for the past decade with the "father of functional medicine," Dr. Jeffrey Bland, as her mentor, and has served on the Nutrition Advisory Board for the Institute of Functional Medicine. Her academic background is in nutritional science, including a Master's Degree in Human Nutrition and Dietetics from the University of Illinois at Chicago (1995), and a Ph.D. in Medical Sciences (Nutrition) from the University of Groningen in The Netherlands (1999). In conjunction with her academic degrees and extensive teaching experience at the university level, she is both a Fellow (F.A.C.N.) and a Certified Nutrition Specialist (C.N.S.) through the American College of Nutrition and has received education in functional medicine through the Institute of Functional Medicine. Dr. Minich has over ten years of experience working in both the food and dietary supplement industries with her last position as Vice President of Scientific Affairs at Metagenics, Inc., in which she was responsible for global product launches in addition to serving as a teaching clinician for international audiences of healthcare practitioners. Her current responsibilities as Vice President of Education at the PLMI involve coordination of cutting-edge information and collaboration with opinion leaders in the personalized lifestyle medicine field. She is the author of four books on nutrition, wellness, and psychology, and is passionate in helping others to live well using therapeutic lifestyle changes.