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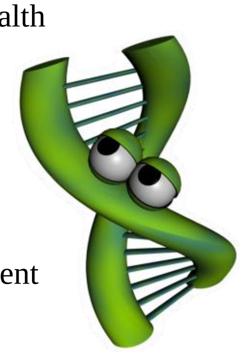
Teacher Background on Epigenetics

What is epigenetics

Epigenetics is the study of the environment's influence on our genes' activity. DNA is often referred to as the blueprint or instruction manual for our bodies. DNA is the hardware, but epigenetics are the software. Epigenetics tell our bodies which section of the blueprint (or which page of the instruction manual) to read at a given time. Epigenetic changes do not alter the letters of our DNA, but instead change its punctuation – think like an exclamation point (!), **bold,** ~~strikethrough~~, footnote, or comma (i.e. "Let's eat Grandpa." this phrase with an epigenetic change might be "Let's eat, Grandpa").

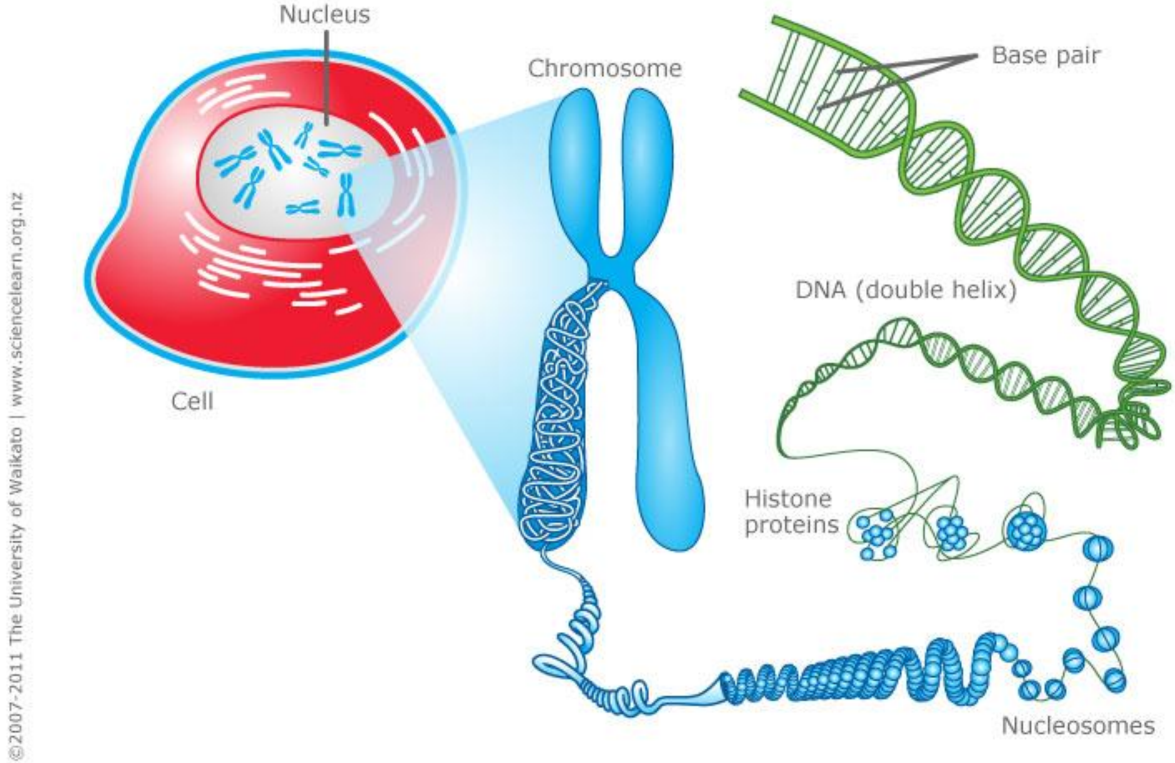
Why is it important

These "punctuation" changes can turn genes "on" or "off", a process called gene regulation. Gene regulation is required for normal development throughout our lives. Genes that are expressed instruct cells what to become, how our organs form, how we remember material for a math test, how our bodies respond to disease and infection, and much, much more. Epigenetics is the study of how environmental factors impact gene regulation which controls gene expression. Gene regulation influences our health throughout our lifespan and new research is suggesting that epigenetic changes may extend across multiple generations to affect the health of our children, grandchildren, and possibly even great-grandchildren. Epigenetic changes are reversible, so our life choices may reverse or mitigate the effects of early epigenetic marks and prevent them from being transmitted to further generations. This is like playing a card game. Even if you are dealt a bad hand it is possible to play it well. It is also possible to mess up a good hand with the wrong life choices. This is an important concept for adolescents because it suggests that we aren't just a product of our genes, but our environment and the choices that we make, too. We need to "nurture our nature".



How does it work? — Molecular Mechanisms

The mechanism of how epigenetics works is fascinating. Stretched end to end, our DNA is about 6 feet long (2 meters) and shoved into practically every cell in our bodies. It is shaped like a long ladder, twisted like a spiral staircase, then wrapped around proteins (histones) like string around spools (see diagram on next page). These wrappings (nucleosomes) are then further condensed into chromosomes. Think of our DNA like a set of encyclopedias where each chromosome is one of its volumes. If you want to "read" any of the instructions contained in one of these volumes, you need to "unfold" the DNA. Not all the DNA can be unwound at the same time, so only parts of the instructions can be accessed at any one time. Only 2-3% of our DNA is made up of genes. Genes are the instructions to make proteins (called gene expression) that make our body function. The remaining 97% of our DNA was previously thought to be "junk DNA" with no known function, though the Encyclopedia of DNA Elements Project (ENCODE) found in 2012 that at least 80% of our genome is active at some point during our lives and is likely involved with regulating gene activity.



http://www.sciencelearn.org.nz/var/sciencelearn/storage/images/contexts/uniquely-me/sci-media/images/cell-chromosomes-and-dna/464336-1-eng-NZ/Cell-chromosomes-and-DNA.jpg

Epigenetics works by 'tagging' or making punctuation changes to our DNA. Two of the best known mechanisms are:

- *Histone acetylation* -- DNA is wound around chemical spools called histones. This saves space in the cell, but tightly wrapped DNA can't be read for gene expression. Chemical triggers can attach an "acetyl group" to an external part of the spool core that causes the core to open the DNA and make it available to reading. Histone acetylation refers to more gene access. Histone deacetylation removes the acetyl group and closes the DNA, so less gene access.
- *DNA Methylation* -- In other cases, a methyl group can be added to the DNA to "tag" it. With several methyl groups added, machinery cannot access the DNA to read it and the resulting gene is not expressed. This serves as a chemical "skip this part". Methyl tags can be added or removed throughout the lifespan by various environmental factors discussed below.
- *Note*: Research is constantly finding new epigenetic mechanisms. For example, histones can be methylated or acetylated in different loci for different functions. RNA was recently found to be methylatable, too. But, the general thought is the same. Epigenetics is all about turning gene activity up or down, on or off.

How is a person impacted by epigenetics

Epigenetics affects our bodies throughout our lives because gene expression occurs every day throughout our lifespan. The epigenetic effects on our health depend on when (in our development) and where (in our bodies) our genes are turned "on" and "off". We have learned from historical famines and population-wide studies that long-term health effects can be observed following a variety of environmental exposures. Current research suggests that the following environmental factors can affect how our genes are regulated.

Sun (ultraviolet light)
Drinking water pollutants
Auto exhaust
Radiation
Diet (methionine, choline, folate, B12)
Hormones (bisphenol A, DES, estrogen, dioxins)
Pesticides
Metals (Ni, Cr, As, Cd, Hg)
Tobacco Smoke
Social interaction

Fetal development

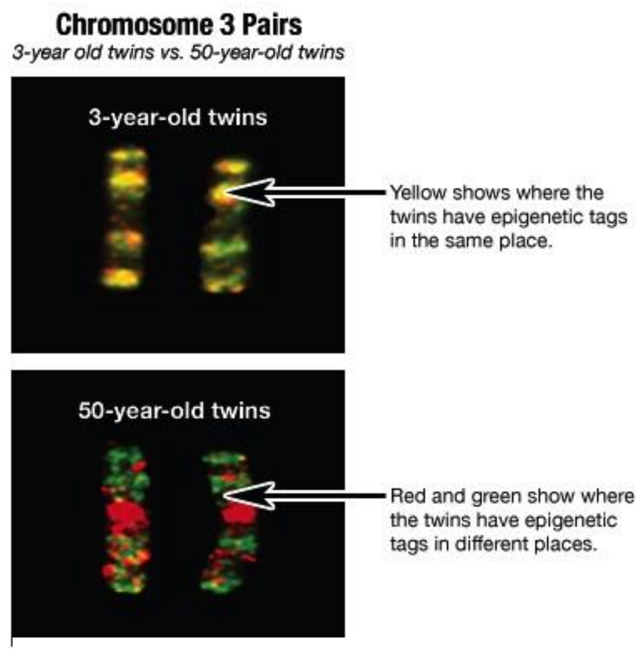
The experience of a fetus in the womb is a critical time for affecting development and future disease risk. For example, our kidneys are normally formed in the womb between 33 and 36 weeks. We now understand that if diet, toxins or other environmental factors disrupt growth during that critical period, the kidney cells won't form properly and health effects can be seen later in adulthood due to low-functioning kidneys. Kidney problems can also be seen earlier in childhood, depending on the extent of the disruption. Research is now finding that there are "developmental origins of disease", where the surrounding environment of the growing baby can affect its susceptibility to chronic disease later in life. Adult risks for obesity, cardiovascular disease, diabetes and metabolic syndrome have been linked to these early fetal development periods. Interestingly birth weight seems to be predictive of this effect, where low birth weight babies have a higher risk of obesity later in life. Babies born around eight-nine pounds seem to have the lowest risk of future disease risk. The increased risk doesn't just happen in low birth weight babies but in high birth weight babies, which may not have had the right nutrients. This "over fed, undernourished" syndrome is a special concern and is currently being studied. We have learned that effects that occur during pregnancy may persist for generations because a female's eggs are all developed during a short time that she is in her mother's womb. These eggs will become the sons and daughters of the baby girl. The nutrition during pregnancy can not only effect a woman's baby, but also her grandchildren. Men aren't immune to this as new evidence is suggesting epigenetic effects may occur on the sperm as well.

Early life epigenetics

A newborn or toddler exposed to bis-phenol A (a chemical formerly used in plastic bottles and still used in the lining of tin cans) becomes vulnerable to obesity in later life. Research in rats has also shown that young rat pups groomed (licked) more frequently by their mothers had a better ability to handle stress as adults than pups groomed less frequently, a result of epigenetic control of glucocorticoid (stress) genes in the brain. Research is currently underway related to how other social interactions can affect our health – bullying, growing up with siblings, abuse, etc. A 2012 paper by Tung and colleagues showed that the dominance rank of rhesus macaques (a type of primate) was strongly associated with gene expression in their immune system, with the magnitude of gene expression actually predicting the macaques' rank in their group over time. This effect hasn't been explored in humans, though it highlights an important biological mechanism for how our physiology and health can interact.

Epigenetics in later life

It is fairly easy to see how something a person is exposed to might modify their epigenome. Identical twins have been used most frequently to study the long-term effects of the environment on our genes since they share the same DNA. When identical twins are young, their epigenetic tags are mostly the same. But as they age and experience different lives, their epigenetic tags are different (see image on right). Likewise, with our different environmental exposures as we age, current cancer research is looking at the epigenetic control of genes related to cell growth that may have been improperly turned "on" or "off" by the environment.



http://learn.genetics.utah.edu/content/epigenetics/twins/

Future research and unanswered questions

There are bound to be many news stories about epigenetics in the next few years. It is important to consider the credibility of the sources of these stories. Carefully designed studies from respected institutions with a clear statement of the limitations of the investigation backed up through review of other scientists are more credible than extreme claims made through the popular press without details of how the investigation was conducted or reviewed. Especially suspicious are claims made in relation to products which claim to have health benefits through epigenetic effects. Other than general dietary recommendations, it is just too early to be able to manufacture such products. Such things will take a number of years of development and would be tested in carefully controlled studies. Currently, there is solid scientific evidence of epigenetic impacts on vulnerability to hypertension, kidney disease, obesity, type II diabetes, cholesterol problems, stroke, and osteoporosis. Under investigation are links between epigenetics and vulnerability to autism, depression, and schizophrenia. Right now, the best advice is to eat a healthy diet, sleep well, avoid stress, and avoid exposure to environmental toxins. All these are familiar bits of advice that your grandmother may have given you, but now we are beginning to understand the deep molecular biology for how they work and we will be able to use that understanding to give more specific epigenetic help.

For more information on genetics or epigenetics, visit the Genetic Science Learning Center http://learn.genetics.utah.edu and http://teach.genetics.utah.edu

Online Resources for Epigenetics

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VIDEO Title	**Source**	**Link**
Epigenetics	PBS - NOVA	http://www.pbs.org/wgbh/nova/body/epigenetics.html
Epigenetics I and II	PBS - NOVA (via youtube)	http://www.youtube.com/watch?v=wFsxVkuChdU (7: http://www.youtube.com/watch?v=Xjq5eEslJhw (6:19)
Epigenetics	scishow (via Youtube)	http://www.youtube.com/watch?v=kp1bZEUgqVI&feature=youtube_gdata_player
Epigenetics makes you unique: Courtney Griffins at TEDxOU	TEDxTALKS (via Youtube)	http://www.youtube.com/watch?v=JTBg6hqeuTg
(Audio slide show) *A Tale of Two Mice*	PBS – NOVA	http://www.pbs.org/wgbh/nova/body/epigenetic-mice.html Audio slide show and supporting web page about the aguti mice and epigenetics.
ARTICLES Title	**Source**	**Link**
How the First Nine Months Shape the Rest of Your Life	Time Magazine - By Annie Murphy Paul	http://www.time.com/time/magazine/article/0,9171,2021065,00.html#ixzz2Wn5nO1wE
Why Your DNA Isn't Your Destiny.	Time Magazine - By John Cloud	http://www.time.com/time/magazine/article/0,9171,1952313,00.html
Beyond DNA: Epigenetics - Deciphering the link between nature and nurture.	Natural History - By Nessa Carey	http://www.naturalhistorymag.com/features/142195/beyond-dna-epigenetics
Epigenetics: Tales of Adversity.	Nature - International Weekly Journal of Science	http://www.nature.com/nature/journal/v468/n7327_supp/full/468S20a.html
WEB SITES Title	**Source**	**Link**
Learn Genetics and Teach Genetics	The University of Utah - Genetic Science Learning Center	http://learn.genetics.utah.edu/content/epigenetics/