Divide and Conquer

Group Summarizing

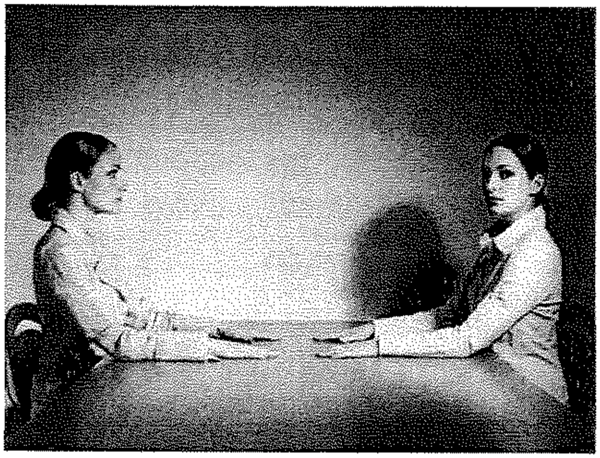
Directions: Choose one of the subtopics or subheadings of material you have just read. Reread that section only. Take notes that summarize the main ideas of that section. Be prepared to teach the rest of the class what you found. As another classmate summarizes his or her section, take notes from their presentation.

Subtopic 1: ____________________	Subtopic 2: ____________________
Subtopic 3: ____________________	Subtopic 4: ____________________

How Epigenetics Works

by Robert Lamb

Browse the article **How Epigenetics Works**



If twins inherit the same set of genes, how can they be so different?
A.B./Photonica/Getty Images

Introduction to How Epigenetics Works

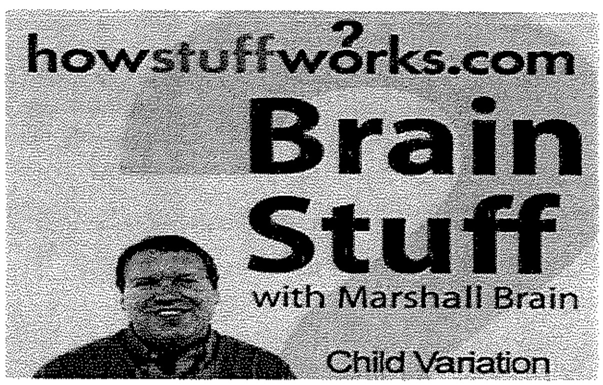
Unless you happen either to have an identical sibling or to know a pair, there's a good chance your knowledge of twins is based in part on fiction. They're everywhere in sub, pulp and popular culture, and it's hard to blame the artists for dragging them into the picture. After all, for a species obsessed with identity, is there a more tantalizing enigma than looking across a table at a physical duplicate of yourself?

If you've seen even a few fictional portrayals of twins, you've probably noticed that the presentation tends to lean toward one extreme or the other. Either the twins are eerily alike (such as the little girls in "The Shining") or remarkably different (such as the dominant and submissive twin gynecologists in "Dead Ringers"). When two human beings look so similar, the things that make them different are just as perplexing as those that make them alike.

DNA plays a central role in modern conceptions of identity, but as our understanding of genetic science improves, so too does our understanding of what makes us who we are. Humans have long engaged in a debate of nature versus nurture, a dilemma with undertones of fate versus freewill. Are you the person you are because you were born that way or because of the world in which you've been brought up?

Obviously, if one identical twin grows up in the castle slums and the other grows up in the king's palace, they're liable to develop into rather different people, no matter how similar their genes are. The field of **epigenetics** adds new fuel to this issue by shedding light on how environment, nutrition and social conditions affect how genes are expressed. Was the twin in the palace brought up by an abusive stepmother? Did the twin in the slums have to contend with a house full of pipe smoke? Did one eat gruel while the other feasted on fatty desserts? These factors can cause epigenetic changes that alter how each twin's genes are expressed. Even a difference in diet could put one twin at risk for cancer and leave the other in the clear.

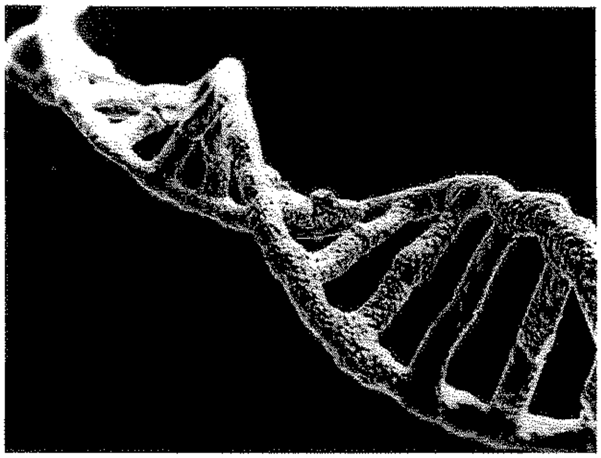
In this article, we'll examine just how this fascinating field of genetics works, how epigenetic changes affect our lives and what the future may hold.



Launch Video

Methylation: From Genome to Phenotype

Have you ever played a flight simulator video game? The game may have offered various realism settings that allow gamers to choose just how "real" their gaming experience will be. Often, you can switch midair collisions on and off, or decide whether you can run out of



DNA may provide a genetic plan for you, but various factors affect how that plan will be expressed.
3D4Medical.com/3D4Medical.com/Getty Images

ammo or gas. The default settings may fall somewhere between pure simulator and arcade shoot-'em-up, but the game has the potential to be more realistic, depending on whether you flip on the appropriate options.

As it turns out, our genes work in a very similar way. If our accumulated genetic material (or **genome**) serves as our program, our gaming experience is our **phenotype**, an organism's observable characteristics. A host of factors, in turn, causes the epigenetic processes that flip different genes on and off.

Scientists first coined the term "epigenetic" (which literally means "above the genome") in the 1940s as a way of classifying changes that occurred between genome and phenotype. For instance, why would only one identical twin develop cancer and not both? In a quest to understand what was happening, scientists looked more closely at the relationship between DNA and cellular development.

DNA resides inside the nucleus of a cell, a master program in the center of every minute piece that makes us who we are. Enzymes attach carbon and hydrogen bundles (CH_3) called **methyl groups** to the DNA, often near the beginning of a gene – the same place where proteins attach to activate the gene. If the protein can't attach due to a blocking methyl group, then the gene usually remains off. Scientists call this particular epigenetic process **methylation**. The arrangement of these bundles can change drastically in the course of a lifetime, but also can set permanently during embryo development. It all depends on the various factors that can affect the distribution of methyl groups.

While epigenetic scientists have devoted most of their research to methylation, they've identified many different types of epigenetic processes. **Chromatin modification** figures heavily among these processes. Inside the nucleus, DNA coils around bundles of **histone** proteins to form **chromatin**, which in turn forms chromosomes. Alter the structure of the chromatin and you alter gene expression. Various chemical groups achieve this end by attaching to the histones.

How does all this influence the nature versus nurture debate? Find out on the next page.

BRUSH UP ON DNA

Are you a little fuzzy on genetic research? Let us break it all down for you in How DNA Works and How Cells Work.

Are we enslaved to our genes that we get from our parents, or can we break free with epigenetic change?
Hauke Dressler/LOOK/Getty Images

The Epigenetic Spin on Nature versus Nurture

It's half time in the big nature versus nurture playoff. Let's run down the score. The fact that we're based in large part on the genes we inherit from our parents is certainly a point for nature, but the fact that our day-to-day life can influence epigenetic changes certainly puts one up on the board for nurture. Interestingly, the next little fact doesn't break the tie – it scores a point for both sides. Based on what we know now, it seems at least some epigenetic changes are hereditary.

Go back to the video game analogy for a moment. Your parents don't just pass on the central program to you, but some of the actual game settings they used. Some chromatin modifications transfer to newly synthesized DNA and proteins. As you might imagine, the prospect of inherited epigenetic changes is having a huge impact on our understanding of evolution. Scientists have even re-evaluated theories they had previously discredited, such as those of 18th-century scientist Jean-Baptiste Lamarck. While recent findings don't completely support Lamarck's theory that the necks of giraffes elongated over the course of generations of reaching for food, some of the evidence is certainly Lamarckian.

Take the water flea for instance. In a predator-heavy environment, the creatures develop large, defensive spines – a trait their offspring also develop, even if raised in a predator-free setting. This process is called **transgenerational epigenetic inheritance**. Humans may not have to contend with growing defensive spines because dad felt threatened, but studies have shown that various behavior and health conditions are due to inherited epigenetic changes.

Epigenetic changes also allow **stem cells** to develop into specialized cells, such as those found in the brain. While organisms depend on this vital process, epigenetic changes also contribute to diseases. In some cases, the gene or genes that are turned on are those associated with debilitating diseases, such as **Angelman syndrome**. In other cases, epigenetic changes turn off a really important gene. To use the video game example again, there's a certain range of settings that work well for an organism, but turning on too few or too many options can lead to a very unsatisfying playing experience. Scientists even think both decreases and increases in **methylation** (chemical bundles that enzymes attach to DNA) may cause cancer, by turning on too many growth-promoting genes or turning off tumor-suppressing genes.

What kinds of factors flip these epigenetic switches? Find out on the next page.

Flipping the Genetic Switch: Epigenetic Factors

The more you look at epigenetics, the more it seems that our lives are little more than a

How much is at stake in your dietary choices? Perhaps more than you think, given the nutritional factors involved in epigenetic change.
Influx Productions/The Image Bank/Getty Images

checklist of various genes that can be turned on or off. Don't want to age as fast? Click here. Care for a little obesity? Just mark "yes" or "no" with a No. 2 pencil. Of course, the kicker is that we're still trying to figure out what factors lead to which answers on the genetic Scantron sheets that define our lives.

Epigenetic changes, like so many of our vital processes, fall to our bodies to deal with. Just think back to the last time you burned dinner or wore the wrong socks to work. Do you really want direct control over your heartbeat or how your genes are expressed? No, so your body responds to your environment and takes care of all this for you. Meanwhile, your brain (which is to say, you) gets to concern itself with such essential problem-solving tasks as gathering food, breeding and remembering to turn off the iron. In our free time, however, we've devoted a great deal of effort to figuring out just how our bodies do what they do. As such, we've already figured out how some factors cause epigenetic changes.

Nutrition: As the saying goes,. you are what you eat. Research has shown that shortages or excesses of food during a person's childhood can cause epigenetic changes that lead to diabetes, obesity and early puberty. Adaptations that made sense during a time of famine can then transfer to children and grandchildren who live in a time of plenty. Genes become epigenetically set to deal with adverse conditions and then pass on to offspring who may enjoy comfier conditions. Experiments have also shown how foods can cause epigenetic changes in the womb. Scientists have influenced coat colors and deterred obesity in mice by feeding the mother a soy-rich diet, which alters methylation [source: Ray].

Parenting: The field of epigenetics continues to shed light on the importance of parental care to mental health. Experiments have discovered that mother rats that infrequently groom and nurse their pups rear anxious offspring. This poor parenting actually alters genes controlling the production of stress hormones. This is nature's way of preparing young for a potentially dangerous environment. In humans, scientists have observed methylation changes in the brains of suicide victims. Areas of the **hippocampus**, a part of the brain that can affect mood, contained genes that had been switched off. An estimated one out of every five suicide victims suffered child abuse, leading experts to consider a possible correlation between stressful upbringings and epigenetic change [source: Economist].

Research continues to uncover connections between epigenetic change and various factors in our environments and diets. How can we benefit from this knowledge? Find out on the next page.

DADS, COCAINE AND FUNGICIDE

Mothers aren't the only ones who pass epigenetic changes to offspring. Experiments with rats have shown the crop fungicide vinclozolin can cause susceptibility to cancer and kidney defects, both of which can be transferred to offspring through methylation changes. In a similar medical experiment, researchers discovered that cocaine-using mice passed memory problems on to three generations of descendants thanks to epigenetic changes.

A scientific researcher extracts the RNA from embryonic stem cells in a laboratory, at the University of Sao Paulo's human genome research center in Brazil.
Mauricio Lima/AFP/Getty Images

The Future of Epigenetics

As knowledge of the epigenome grows, we continue to learn more about how the substances we consume and the social situations we inhabit influence the way our genes are expressed. Scientists are already rethinking the way organisms evolve and how traits are passed on from parent to offspring. But at what point will this knowledge begin to change the way we live? At what point will we be able to take a pill and block or unblock the right combination of genes to improve our quality of life?

While turning off aging and fine-tuning the human genome are pretty awe-inspiring possibilities, epigeneticists are far more interested in discovering ways to treat epigenetic diseases. As some cancers occur due to the deactivation of tumor-suppressing genes, researchers have worked to develop medications that reactivate them. The drug azacitidine, for instance, treats leukemia in this manner. Finding just the right parts of the epigenome to treat, however, can be like finding a needle in a haystack. And once researchers find the areas they want to affect, epigenetic drugs aren't all that specific. They might succeed in blocking or unblocking the genes they wanted to treat, but also affect other genes, resulting in potentially dangerous side effects.

Following the completion of the Human Genome Project, the **Human Epigenome Project** is currently striving to map the scope of changes that can occur between genome and phenotype. Once finished, however, an epigenomic map could also prove useful in determining which individuals are at risk for certain diseases and encouraging the kind of lifestyle changes that can prevent the wrong genes from switching on or off.

More than future medicines are at stake, however. Epigenetic discoveries also force doctors to reexamine existing drugs. Even azacitidine, the first FDA-approved epigenomic drug, was used previously to treat bone-marrow stem cell disorders. It was only after the discovery of its epigenetic effects that doctors explored its uses in other areas.

Stem cells are also of key interest to epigeneticists. By studying the epigenetic changes that determine how cells develop, it may eventually become possible to dictate what tissue type a stem cell will develop into. For more information on the implications of this, read How Stem Cells Work.

In the meantime, the more we know about epigenetic changes, the more we realize the correlation between our actions and, not only our own lives, but the lives of our children. As we peel away another genetic layer to find out who we are, what other mysteries await us?

Follow the links on the next page to learn even more about DNA.

Lots More Information

Related HowStuffWorks Articles

- What is the Human Epigenome Project?
- How Cancer Works
- How Cells Work
- How Designer Children Will Work
- How DNA Works
- How Stem Cells Work
- Would having your own clone be like having an identical twin?

More Great Links

- The Human Epigenome Consortium

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