CHAPTER TEN

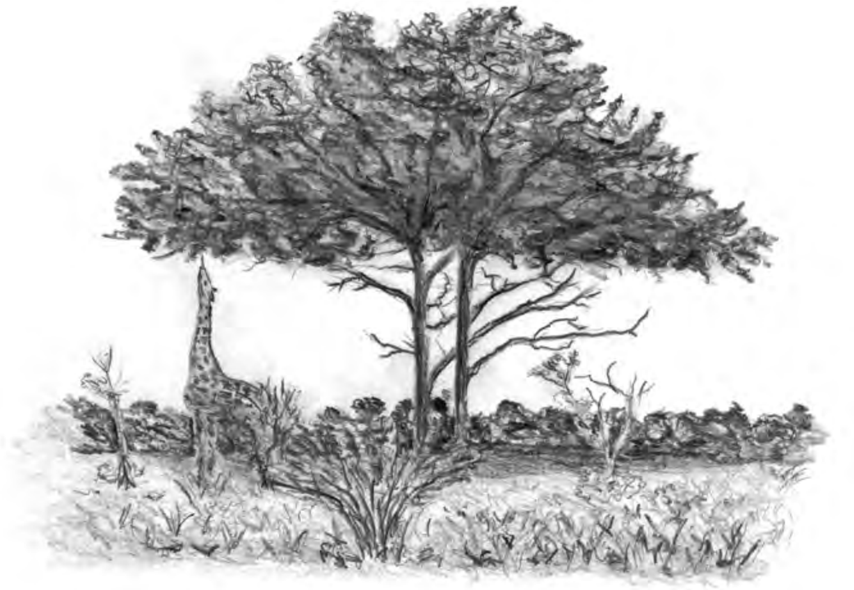
Genes 2.1—How to Improve Your Genes

We have long understood that lifestyle cannot alter heredity. But it turns out that it can . . .

Over the last century, few scientists' names have been subjected to as much historical derision as early-nineteenth-century French biologist Jean-Baptiste de Lamarck. In textbooks and elsewhere, Lamarckism has been defined (and mocked) as a crude, pre-Darwinian conception of evolution, tainted by the flimsy idea that biological heredity can somehow be altered through personal experience.

Lamarck called it "the inheritance of acquired characteristics"—the notion that an individual's actions can alter the biological inheritance passed on to his or her children. For example, giraffes, according to Lamarck's theory, had developed longer and longer necks over the generations because of the giraffe's practice of reaching higher and higher for food.

> The giraffe is . . . obliged to browse on the leaves of trees and to make constant efforts to reach them. From this habit long maintained in all its race, it has resulted that the animal's forelegs have become longer than its hind-legs, and that its neck is lengthened.
>
> —JEAN-BAPTISTE DE LAMARCK, *Philosophie Zoologique*, 1809



This sounds preposterous to us now, mostly because it is so different from our Darwinian understanding of evolution. After Darwin's *Origin of Species* and others' subsequent discovery of genes, a very different notion—the theory of natural selection—became scientific and popular consensus. For more than a century, it has been universally accepted that genes are altered not by individual experience but by random mutation and other factors. The individuals whose mutations happen to best fit their environments will thrive and will pass their genes on to future generations.

We cannot change our genes. In the 1950s, the discovery of DNA reaffirmed this idea and secured Lamarck's place in history as the intellectual loser. Today, any high school student knows that genes are passed on unchanged from parent to child, and to the next generation and the next. Lifestyle *cannot* alter heredity.

Except now it turns out that it can . . .

. . .

In 1999, botanist Enrico Coen and his colleagues at the United Kingdom's John Innes Centre were trying to isolate the genetic differences between two distinct types of the toadflax plant. The newer and rarer type,

Newer "Peloria" toadflax

EMIL NILSSON

Ordinary toadflax

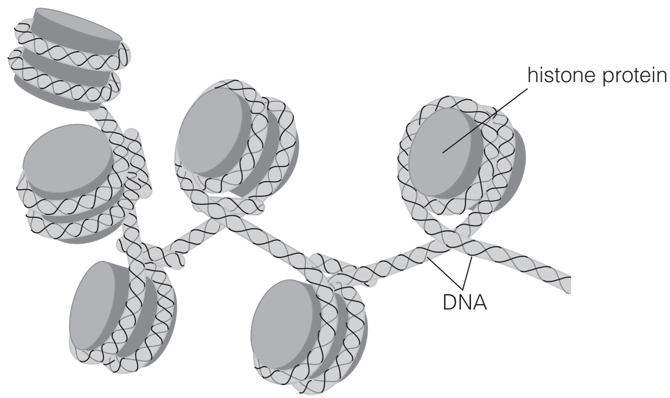
named "Peloria" (left, above) by Carl Linnaeus in the mid-eighteenth century, has a distinct type of flower with five spurs surrounding it like a star.

The trouble was, this difference couldn't be found on the genes. When they looked closely at the gene known to be associated with flower symmetry, a gene known as *Lcyc*, Coen's team was astounded to find that the DNA code in each plant was exactly the same. Two very distinct flowers, same genetic code.

What they discovered next was even more surprising. There *was* a difference between the two flowers on their respective *epigenomes*—the packaging that surrounds DNA.

Some quick background on genetic architecture: DNA is famously wound together in a double-helix strand that, close-up (at a magnification of about 10 million times), looks like this:

From farther away, those same DNA strands look much smaller, of course, and one can see that each strand is coiled around a protective packaging of histone proteins, which (at a magnification of about 1 million times) looks like this:



These histones protect the DNA and keep it compact. They also serve as a mediator for gene expression, telling genes when to turn on and off. It's been known for many years that this epigenome ("epi-" is a Latin prefix for "above" or "outside") can be altered by the environment and is therefore an important mechanism for gene-environment interaction.

What scientists didn't realize, though, was that changes to the epigenome can be inherited. Prior to 1999, everyone thought that the epigenome was always wiped clean like a blackboard with each new generation.

Not so, discovered Enrico Coen. In the case of the Peloria toadflax flower, a clear alteration to the epigenome had subsequently been passed down through many generations.

And it wasn't just flowers. That same year, Australian geneticists Daniel Morgan and Emma Whitelaw made a very similar discovery in mice. They observed that their batch of genetically identical mice were turning up with a range of different fur colors—differences traced back to epigenetic alterations and passed on to subsequent generations. What's more, they and other researchers discovered that these fur-color epigenes could be manipulated by something as basic as food. A pregnant yellow mouse eating a diet rich in folic acid or soy milk would be prone to experience an epigenetic mutation producing brown-fur offspring, and even with the pups returning to a normal diet, that brown fur would be passed to future generations.

After that, more epigenetic discoveries piled in one after another:

- In 2004, Washington State University's Michael Skinner discovered that exposure to a pesticide in one generation of rats spurred an epigenetic change that led to low sperm counts lasting at least four generations.
- In 2005, New York University's Dolores Malaspina and colleagues discovered age-related epigenetic changes in human males that can lead to lower intelligence and a higher risk of schizophrenia in children.
- In 2006, London geneticist Marcus Pembrey presented data from Swedish medical records to show that nutritional deficiencies and cigarette smoking in one generation of humans had effects across several generations.
- In 2007, the Institute of Child Health's Megan Hitchins and colleagues reported a link between inherited epigenetic changes and human colon cancer.

Welcome back, Monsieur Lamarck! "Epigenetics is proving we have some responsibility for the integrity of our genome," says the Director of Epigenetics and Imprinting at Duke University, Randy Jirtle. "Before, [we thought that] genes predetermined outcomes. Now [we realize that] everything we do—everything we eat or smoke—can affect our gene expression and that of future generations. Epigenetics introduces the concept of free will into our idea of genetics."

And that of future generations. This is big, big stuff—perhaps the most important discovery in the science of heredity since the gene.

No one can yet measure the precise implications of these discoveries, because so little is known. But it is already clear that epigenetics is going to radically alter our understanding of disease, human abilities, and evolution. It begins with this simple but utterly breathtaking concept:

Lifestyle* can *alter heredity.

Lamarck was probably not correct about the giraffe in particular, and he was certainly wrong about inherited characteristics being the primary vehicle of evolution. But in its most basic form, his idea that what an individual does in his/her life before having children can change the biological inheritance of those children and their descendants—on this he turns out to have been correct. (And two hundred years ahead of everyone else.) Quietly, biologists have come to accept in recent years that biological heredity and evolution is a lot more intricate than we once thought. The concept of inherited epigenetic changes certainly does not invalidate the theory of natural selection, but it makes it a lot more complicated. It offers not just another mechanism by which species can adapt to changing environments, but also the prospect of an evolutionary process that is more interactive, less random, and runs along several different parallel tracks at the same time. "DNA is not the be all and end all of heredity," write geneticists Eva Jablonka and Marion Lamb. "Information is transferred from one generation to the next by many interacting inheritance systems. Moreover, contrary to current dogma, the variation on which natural selection acts is not always random . . . new heritable variation can arise in response to the conditions of life."

How do these recent findings impact our understanding of talent and intelligence? We can't yet exactly be sure. But the door of possibility is wide-open. If a geneticist had suggested as recently as the 1990s that a twelve-year-old kid could improve the intellectual nimbleness of his or her future children by studying harder now, that scientist would have been laughed right out of the conference hall. Today, that preposterous scenario looks downright likely:

> Washington, D.C.—New animal research in the February 4 [2009] issue of *The Journal of Neuroscience* shows that a stimulating environment improved the memory of young mice with a memory-impairing genetic defect and also improved the memory of their eventual offspring. The findings suggest that *parental behaviors that occur long before pregnancy may influence an offspring's well-being.* "While it has been shown in humans and in animal models that enriched experience can enhance brain function and plasticity, this study is a step forward, suggesting that the enhanced learning behavior and plasticity can be transmitted to offspring long before the

> pregnancy of the mother," said Li-Huei Tsai, PhD, at Massachusetts Institute of Technology and an investigator of the Howard Hughes Medical Institute, an expert unaffiliated with the current study.

In other words, we may well be able to improve the conditions for our grandchildren by putting our young children through intellectual calisthenics now.

What else is possible? Could a family's dedication to athletics in one or more generations induce biological advantages in subsequent generations?

Could a teenager's musical training improve the "musical ear" of his great-grandchildren?

Could our individual actions be affecting evolution in all sorts of unseen ways?

"People used to think that once your epigenetic code was laid down in early development, that was it for life," says McGill University epigenetics pioneer Moshe Szyf. "But life is changing all the time, and the epigenetic code that controls your DNA is turning out to be the mechanism through which we change along with it. Epigenetics tells us that little things in life can have an effect of great magnitude."

Everything we know about epigenetics so far fits perfectly with the dynamic systems model of human ability. Genes do not dictate what we are to become, but instead are actors in a dynamic process. Genetic expression is modulated by outside forces. "Inheritance" comes in many different forms: we inherit stable genes, but also alterable epigenes; we inherit languages, ideas, attitudes, but can also change them. We inherit an ecosystem, but can also change it.

Everything shapes us and everything can be shaped by us. The genius in all of us is our built-in ability to improve ourselves and our world.