CHAPTER ONE

Genes 2.0

How Genes Really Work

Contrary to what we've been taught, genes do not determine physical and character traits on their own. Rather, they interact with the environment in a dynamic, ongoing process that produces and continually refines an individual.

The sun begins to rise over an old river town, and through a fifth-floor window of University Hospital, a newborn cries out her own birth announcement. Her new, already sleep-deprived parents hold her tightly and simply stare, partly in disbelief that this has actually happened, partly in awe of what lies ahead. As she develops, who will she look like? What will she be like? What will be her strengths, her weaknesses? Will she change the world or just scrape by? Will she run a quick mile, paint a new idea, charm her friends, sing for millions? Will she have any talent for anything?

Only the years will tell. For right now, the parents don't really need to know the final outcome—they just need to know what sort of difference they can make. How much of their newborn daughter's personality and abilities are already predetermined? What portion is still up for grabs? What ingredients can they add, and what tactics should they avoid?

The fuzzy mix of hope, expectation, and burden begins . . .

TONY SOPRANO: And to think [I'm] the cause of it.
DR. MELFI: How are you the cause of it?
TONY SOPRANO: It's in his blood, this miserable fucking existence. My rotten fucking putrid genes have infected my kid's soul. That's my gift to my son.

Genes can be scary stuff if you don't understand them. In 1994, psychologist Richard Herrnstein and policy analyst Charles Murray warned in their best-selling book *The Bell Curve* that we live in an increasingly stratified world where the "cognitive elite"—those with the best genes—are more and more isolated from the cognitive/genetic underclass. "Genetic partitioning," they called it. There was no mistaking their message:

> The irony is that as America equalizes the [environmental] circumstances of people's lives, the remaining differences in intelligence are increasingly determined by differences in genes . . . Putting it all together, success and failure in the American economy, and all that goes with it, are increasingly a matter of the genes that people inherit.

Stark and terrifying—and thankfully quite mistaken. The authors had fundamentally misinterpreted a number of studies, becoming convinced that roughly 60 percent of each person's intelligence comes directly from his or her genes. But genes don't work that way. "There are no genetic factors that can be studied independently of the environment," explains McGill University's Michael Meaney, one of the world's leading experts on genes and development. "And there are no environmental factors that function independently of the genome. [A trait] emerges only from the *interaction* of gene and environment."

While Herrnstein and Murray adhered to a particular ideological agenda, they also seem to have been genuinely hobbled in their analysis by a common misunderstanding of how genes work. We've all been taught that we inherit complex traits like intelligence straight from our parents' DNA in the same way we inherit simple traits like eye color. This belief is continually reinforced by the popular media. As an illustration, *USA Today* recently explained heredity in this way:

> Think of your own genetic makeup as the hand of cards you were dealt at conception. With each conception in a family comes a new shuffling of the deck and a new hand. That's partly why little Bobby sleeps through the night as a baby, always behaves and seems to love math, while brother Billy is colicky, never listens and already is the head of a gang in kindergarten.

Genes dictate. Genes instruct. Genes determine. For more than a century, this has been the widely accepted explanation of how each of us becomes us. In his famous pea-plant experiments of the 1850s and '60s, Gregor Mendel demonstrated that basic traits like seed shape and flower color were reliably passed from one generation to the next through dominant and recessive "heritable factors" (Mendel's phrase before the word "gene" was introduced). After eight years and twenty-eight thousand plants, Mendel had proved the existence of genes—and seemed to prove that genes alone determined the essence of who we are. Such was the unequivocal interpretation of early-twentieth-century geneticists.

That notion is with us still. "Genes set the stage," affirms *USA Today*. The environment has an impact on all of our lives, to be sure, but genes come first; they set specific lower and upper limits of each person's potential abilities. *Where did your brother get that amazing singing voice? How did you get so tall? Why can't I dance? How is she so quick with numbers?*

"It's in the genes," we say.

That's what *The Bell Curve* authors thought, too. None of these writers realized that over the last two decades Mendel's ideas have been thoroughly upgraded—so much so that one large group of scientists now suggests that we need to wipe the slate clean and construct an entirely new understanding of genes.

This new vanguard is a loose-knit group of geneticists, neuroscientists, cognitive psychologists, and others, some of whom call themselves developmental systems theorists. I call them *interactionists* because of their emphasis on the dynamic interaction between genes and the environment. Not all of the interactionists' views have yet been fully accepted, and they freely acknowledge their ongoing struggle to articulate the full implications of their findings. But it already seems very clear that these implications are far-reaching and paradigm-shifting.

To understand interactionism, you must first try to forget everything you think you know about heredity. "The popular conception of the gene as a simple causal agent is not valid," declare geneticists Eva Jablonka and Marion Lamb. "The gene cannot be seen as an autonomous unit—as a particular stretch of DNA which always produces the same effect. Whether or not a length of DNA produces anything, what it produces, and where and when it produces it may depend on other DNA sequences and on the environment."

Though Mendel couldn't detect it with his perfectly calibrated pea-plant hybrids, genes are not like robot actors who always say the same lines in the exact same way. It turns out that they interact with their surroundings and can say different things depending on whom they are talking to.

This obliterates the long-standing metaphor of genes as blueprints with elaborate predesigned instructions for eye color, thumb size, mathematical quickness, musical sensitivity, etc. Now we can come up with a more accurate metaphor. Rather than finished blueprints, genes—all twenty-two thousand of them[1]—are more like volume knobs and switches. Think of a giant control board inside every cell of your body.

Many of those knobs and switches can be turned up/down/on/off at any time—by another gene or by any minuscule environmental input. This flipping and turning takes place constantly. It begins the moment a child is conceived and doesn't stop until she takes her last breath. Rather than giving us hardwired instructions on how a trait must be expressed, this process of gene-environment interaction drives a unique developmental path for every unique individual.

The new interactionists call it "GxE" for short. It has become central to the understanding of all genetics. Recognition of GxE means that we now

[1] Estimates of the actual number of genes vary.

realize that genes powerfully influence the formation of all traits, from eye color to intelligence, but rarely dictate precisely what those traits will be. From the moment of conception, genes constantly respond to, and interact with, a wide range of internal and external stimuli—nutrition, hormones, sensory input, physical and intellectual activity, and other genes—to produce a unique, custom-tailored human machine for each person's unique circumstance. Genes matter, and genetic differences will result in trait differences, but in the final analysis, each of us is a dynamic system, a creature of development.

This new dynamic model of GxE (genes multiplied by environment) is very different from the old static model of G+E (genes plus environment). Under the old paradigm, genes came first and set the stage. They dealt each of us our first hand of cards, and only afterward could we add in environmental influences.

The new model begins with interaction. There is no genetic foundation that gets laid before the environment enters in; rather, genes express themselves strictly in accordance with their environment. Everything that we are, from the first moment of conception, is a result of this process. We do not *inherit* traits directly from our genes. Instead, we *develop* traits through the dynamic process of gene-environment interaction. In the GxE world, genetic differences still matter enormously. But, on their own, they don't determine who we are.

In fact, you did not even inherit your blue eyes or brown hair from your parents' genes. Not directly.

This may sound crazy at first, because of how thoroughly we've been indoctrinated with Mendelian genetics. The reality turns out to be much more complicated—even for pea plants. Many scientists have understood this much more complicated truth for years but have had trouble explaining it to the general public. It is indeed a lot harder to explain than simple genetic determinism.

. . .

To understand genes more fully, we first need to take a step back and explain what they actually do:

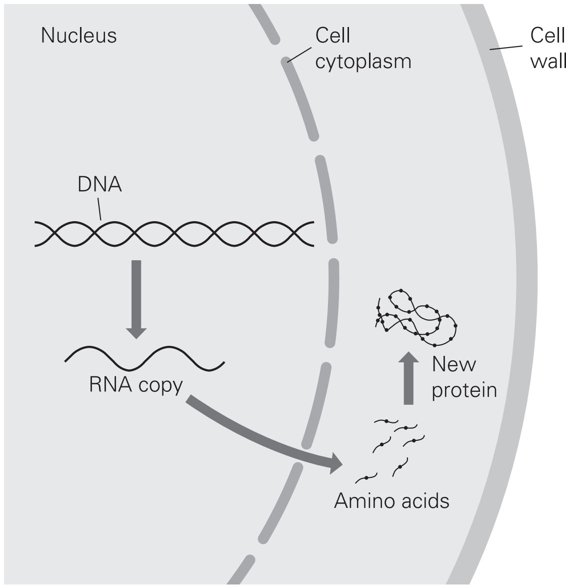
Genes direct the production of proteins.

Each of our cells contains a complete double strand of DNA, which in turn contains thousands of individual genes. Each gene initiates the process of assembling amino acids into proteins. Proteins are large, specialized molecules that help create cells, transport vital elements, and produce necessary chemical reactions. There are many different protein types, and they provide the building blocks of everything from muscle fiber to eyeball collagen to hemoglobin. We are, each one of us, the sum of our proteins.

Genes contain the instructions for the formation of those proteins, and they direct the protein-building process (Diagram A).

But . . . genes are *not* the only things influencing protein construction.

Diagram A



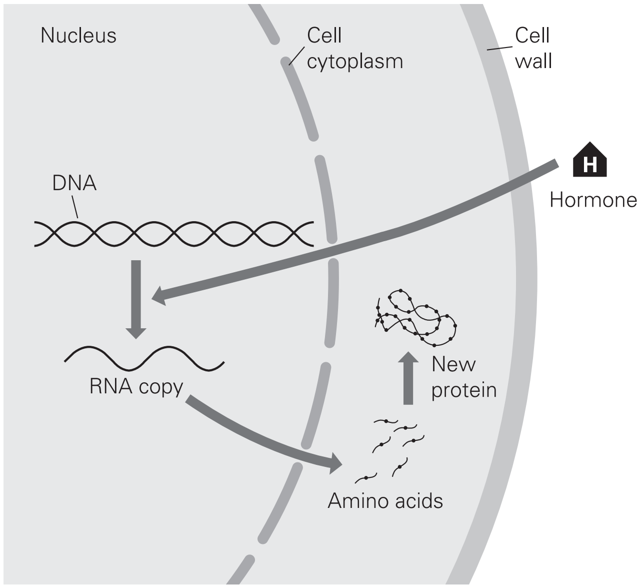
It turns out that the genetic instructions themselves are influenced by other inputs. Genes are constantly activated and deactivated by environmental stimuli, nutrition, hormones, nerve impulses, and other genes (Diagram B).

This explains how every brain cell and hair cell and heart cell in your body can contain *all* of your DNA but still perform very specialized functions. It also explains how a tiny bit of genetic diversity goes a very long way: human beings are distinct from one another not just because of our relatively few genetic differences, but also because every moment of our ongoing lives actively influences our own genetic expression.

Think of GxE as baking a cake, suggests Cambridge University biologist Patrick Bateson. A hundred cooks may start out with nearly the same ingredients but will in the end produce very different cakes. While the slight difference in ingredients guarantees that differences will exist, it doesn't dictate what those differences will be. The actual end-result differences arise out of the process. "Development is chemistry," says Bateson, "and the end product cannot simply be reduced to its ingredients."

Similarly, the mere presence of a certain gene does not automatically produce a specific type or number of proteins. First, every gene has to be

Diagram B



activated—switched on, or "expressed"—in order to initiate protein construction.

Further, geneticists have recently discovered that some genes—we don't yet know how many—are versatile. In some cases, the exact same gene can produce different proteins depending on how and when it is activated.

All of this means that, on their own, most genes cannot be counted on to directly produce specific traits. They are active participants in the developmental process and are built for flexibility. Anyone seeking to describe them as passive instruction manuals is actually minimizing the beauty and power of the genetic design.

So why do I have brown eyes like my mom and red hair like my dad?

In practical terms, there are many elementary physical traits like eye, hair, and skin color where the process is near Mendelian—where certain genes produce predictable outcomes most of the time. But looks can be deceiving; a simple Mendel-like result doesn't mean that there wasn't gene-environment interaction. "Even in the case of eye color," says Patrick Bateson, "the notion that the relevant gene is *the* [only] cause is misconceived, because [of] all the other genetic and environmental ingredients." Indeed, Victor McKusick, the Johns Hopkins geneticist widely regarded as the father of clinical medical genetics, reminds us that in some instances "two blue-eyed parents can produce children with brown eyes." Recessive genes cannot explain such an event; gene-environment interaction can.

When it comes to more complex traits like physical coordination, personality, and verbal intelligence, gene-environment interaction inevitably moves the process even further away from simple Mendelian patterns.

What about single genetic mutations that predictably cause diseases such as Huntington's disease?

Single-gene diseases do exist and account for roughly 5 percent of the total disease burden in developed countries. But it's important not to let such diseases give the wrong impression about how healthy genes work. "A disconnected wire can cause a car to break down," explains Patrick Bateson. "But this does not mean that the wire by itself is responsible for making the car move." Similarly, a genetic defect causing a series of problems does not mean that the healthy version of that gene is single-handedly responsible for normal function.

Helping the public understand gene-environment interaction is a particular burden, because it is so enormously complex. It will never have the same easy, snap-your-fingers resonance that our old (misleading) understanding of genes had for us. Given that, the interactionists are lucky to have Patrick Bateson on their side. A former biological secretary to the Royal Society of London and one of the world's leading public educators about heredity, Bateson also carries a powerful symbolic message with his surname. It was his grandfather's famous cousin, William Bateson, who, a century ago, first coined the word "genetics" and helped popularize the earlier, simpler notion of genes as self-contained information packets that directly produce traits. Now the third-generation Bateson is helping to significantly update that public understanding.

"Genes store information coding for the amino acid sequences of proteins," explains Bateson. "That is all. They do not code for parts of the nervous system and they certainly do not code for particular behavior patterns."

His point is that genes are several steps removed from the process of trait formation. If someone is shot dead with a Smith & Wesson handgun, no one would accuse the guy running the blast furnace that transformed the iron ore into pig iron—which was subsequently transformed into steel and later poured into various molds before being assembled into a Smith & Wesson handgun—of murder. Similarly, no gene has explicit authorship of good or bad vision, long or short legs, or affable or difficult personality. Rather, genes play a crucial role throughout the process. Their information is translated by other actors in the cell and influenced by a wide variety of other signals coming from outside the cell. Certain types of proteins are then formed, which become other cells and tissues and ultimately make us who we are. The step-by-step distance between a gene and a trait will depend on the complexity of the trait. The more complex the trait, the farther any one gene is from direct instruction. This process continues throughout one's entire life.

Height can provide a terrific insight into the gene-environment dynamic. Most of us think of height as being more or less directly genetically determined. The reality is so much more interesting. One of the most striking early hints of the new understanding of development as a dynamic process emerged in 1957 when Stanford School of Medicine researcher William Walter Greulich measured the heights of Japanese children raised in California and compared them to the heights of Japanese children raised in Japan during the same time period. The California-raised kids, with significantly better nourishment and medical care, grew an astonishing five inches taller on average. Same gene pool, different environment—radically different stature. Greulich didn't realize this at the time, but it was a perfect illustration of how genes really work: not dictating any predetermined forms or figures, but interacting vigorously with the outside world to produce an improvised, unique result.

It turns out that a wide variety of environmental elements will affect the genetic expression of height: a single case of diarrhea or measles, for example, or deficiencies in any one of dozens of nutrients. In Western cultures of the twenty-first century, we tend to assume a natural evolutionary trend of increased height with each generation, but in truth human height has fluctuated dramatically over time in specific response to changes in diet, climate, and disease. Most surprising of all, height experts have determined that, biologically, very few ethnic groups are truly destined to be taller or smaller than other groups. While this general rule has some exceptions, "by and large," sums up *The New Yorker*'s Burkhard Bilger, "any population can grow as tall as any other . . . Mexicans ought to be tall and slender. Yet they're so often stunted by poor diet and diseases that we assume they were born to be small."

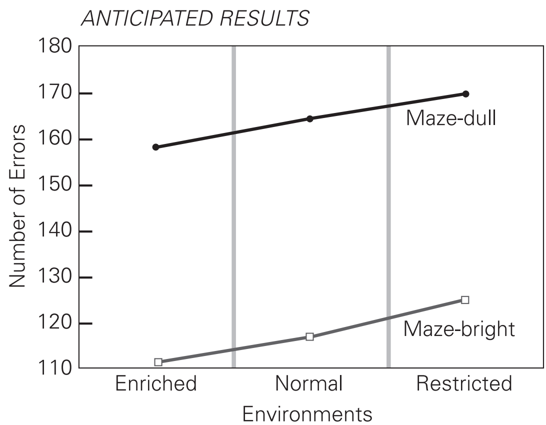
Born to be small. Born to be smart. Born to play music. Born to play basketball. It's a seductive assumption, one that we've all made. But when one looks behind the genetic curtain, it most often turns out not to be true.

Another stunning example of the gene-environment interactive dynamic arrived, coincidentally, just one year after Greulich's Japanese height study. In the winter of 1958, Rod Cooper and John Zubek, two young research psychologists at the University of Manitoba, devised what they thought was a classic nature/nurture experiment about rat intelligence. They started with newborn rat pups from two distinct genetic strains: "Maze-bright" rats, which had consistently tested well in mazes over many generations, and "Maze-dull" rats, which had consistently tested poorly in those same mazes, making an average of 40 percent more mistakes.

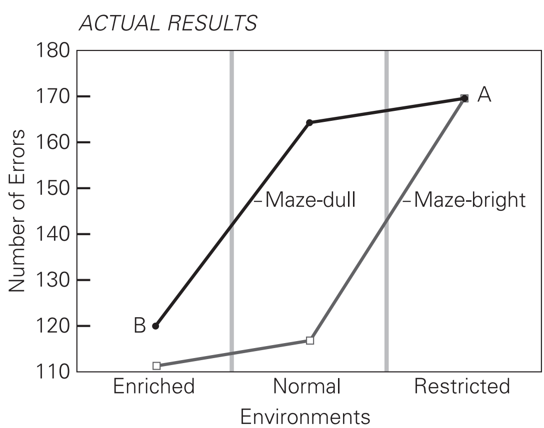
Then they raised each of these two genetic strains in three very different living conditions:

> **Enriched environment:** featuring walls painted in rich, bright patterns and many stimulating toys: ramps, mirrors, swings, slides, bells, etc.
>
> **Normal environment:** with ordinary walls and a moderate amount of exercise and sensory toys.
>
> **Restricted environment:** essentially rat slums with nothing but a food box and a water pan; no toys or anything else to stimulate their bodies or minds.

In broad terms, it seemed easy enough to predict the outcome: each strain of rat would get a little smarter when raised in the enriched environment and get a little dumber when raised in the poor environment. They expected to have a graph that looked something like this:



Instead, the results looked like this:



The final data were quite shocking. Under normal conditions, the Maze-bright rats had consistently outperformed the Maze-dull rats. But in both extreme environments, they performed virtually the same. The Maze-bright rats raised in the restricted environment made almost exactly the same number of mistakes as the Maze-dull rats raised in the restricted environment (point A, above). In other words, when raised in an impoverished environment, all the rats seemed equally dumb. Their "genetic" differences disappeared.

The same thing happened with the enriched environment. Here, the Maze-bright rats also made very close to the same number of mistakes as the Maze-dull rats (point B, above—the difference was deemed statistically insignificant). Raised in an exciting, provocative environment, all the rats seemed equally smart. Again, their "genetic" differences disappeared.

At the time, Cooper and Zubek didn't really know what to make of it. The truth was that these original "genetic" differences hadn't really ever been purely genetic. Rather, they had been a function of each strain's GxE development within its original environment. Now, when developing within different environments, each strain was producing very different results. And in the case of both the enriched and restricted environments, the different genetic strains turned out to be a lot more alike than they had previously seemed.

In the decades that followed, the Cooper-Zubek study emerged as "a classic example of gene-environment interaction," according to Penn State developmental geneticist Gerald McClearn. Many other scientists agree.

Over this same time period, hundreds of examples emerged that gradually forced a wholesale rethinking of how genes operate. Almost in disbelief, biologists observed that

- the temperature surrounding turtle and crocodile eggs determined their gender
- young, yellow-skinned grasshoppers became permanently black skinned for camouflage if exposed to a blackened (burnt) environment at a certain age
- locusts living in a crowded environment developed vastly more musculature (suitable for migration) than locusts living in less crowded conditions

In these and so many other instances, environment A seemed to produce one kind of creature while environment B produced another creature entirely. This level of trait modification was simply impossible to comprehend under the old G+E idea that genes directly determined traits. The new facts demanded a whole new explanation of how genes function.

In 1972, Harvard biologist Richard Lewontin supplied a critical clarification that helped his colleagues understand GxE. The old nature-and-nurture view featured a one-way, additive sequence like this:

Genes->proteins->cells->traits
↗
Environment

Genes trigger the production of proteins, which guide the functions of cells, which, with some input from the outside world, form traits.

The new GxE was a much more dynamic process, with every input at every level influencing every other input:

Genes ↔ proteins->cells->traits
⤡ ⤢
Environment

Genes, proteins, and environmental signals (including human behavior and emotion) constantly interact with one another, and this interactive process influences the production of proteins, which then guide the functions of cells, which form traits.

Note the influence-arrows moving in both directions in the second sequence. "Biologists have come to realise that if one changes *either* the genes *or* the environment, the resulting behaviour can be dramatically different," explains City University of New York evolutionary ecologist Massimo Pigliucci. "The trick, then, is not in partitioning causes between nature and nurture, but in [examining] the way genes and environments interact dialectically to generate an organism's appearance and behaviour."

The great irony, then, of our endless efforts to distinguish nature from nurture is that we instead need to do exactly the opposite: to try to understand precisely how nature and nurture *interact*. Precisely which genes do get switched on, and when, and how often, and in what order, will make all the difference in the function of each cell—and the traits of the organism.

"In each case," explains Patrick Bateson, "the individual animal starts its life with the capacity to develop in a number of distinctly different ways. Like a jukebox, the individual has the potential to play a number of different developmental tunes. But during the course of its life it plays only one tune. The particular developmental tune it does play is selected by [the environment] in which the individual is growing up."

From that first moment of conception, then, our temperament, intelligence, and talent are subject to the developmental process. Genes do not, on their own, make us smart, dumb, sassy, polite, depressed, joyful, musical, tone-deaf, athletic, clumsy, literary, or incurious. Those characteristics come from a complex interplay within a dynamic system. Every day in every way you are helping to shape which genes become active. Your life is interacting with your genes.

The dynamic model of GxE turns out to play a critical role in everything—your mood, your character, your health, your lifestyle, your social and work life. It's how we think, what we eat, whom we marry, how we sleep. The catchy phrase "nature/nurture" sounded good a century ago, but it makes no sense today, since there are no truly separate effects. Genes and the environment are as inseparable and inextricable as letters in a word or parts in a car. We cannot embrace or even understand the new world of talent and intelligence without first integrating this idea into our language and thinking.

We need to replace "nature/nurture" with "dynamic development."

How did Tiger Woods end up with the most dependable stroke and the toughest competitive drive in the history of golf? Dynamic development. How did Leonardo da Vinci develop into an unparalleled artist, engineer, inventor, anatomist, and botanist? Dynamic development. How did Richard Feynman advance from a boy with a merely good IQ score to one of the most important thinkers of the twentieth century? Dynamic development.

Dynamic development is the new paradigm for talent, lifestyle, and well-being. It is how genes influence everything but strictly determine very little. It forces us to rethink everything about ourselves, where we come from, and where we can go. It promises that while we'll never have true control over our lives, we do have the power to impact them enormously. Dynamic development is why human biology is a jukebox with many potential tunes—not specific built-in instructions for a certain kind of life, but built-in capacity for a variety of possible lives. No one is genetically doomed to mediocrity.

Dynamic development was one of the big ideas of the twentieth century, and remains so. Once our brand-new parents in University Hospital understand its implications for their newborn girl, it will affect how they live, how they parent, and even how they vote.