PART ONE

It's Alive!

I'm afraid you're stuck with your genes.
—Dr. Julius Hibbert, "Lisa the Simpson"

[T]here's nothing wrong with the Simpson genes.
—Homer Simpson, "Lisa the Simpson"

1

The Simpson Gene

Mundane families are all alike; every unusual family is unusual in its own way. The Simpsons are emphatically a breed unto themselves. Begin with Homer's fanatical cravings, bizarre non sequiturs, off-the-wall daydreams, childish single-minded pursuits, and overall obliviousness. Add to the lunacy Grandpa's bizarre, rambling stories, full of implausible, inconsistent recollections of World War II, and his wholly unexplained antipathy toward the state of Missouri. Mix in Bart's propensity for utter mischief and absolute disregard for authority. Watch them insult, scream at, and even try to strangle one another. Not even Tolstoy, who wrote much about dysfunctional families, could keep up with all the twists and turns of the crazy plot machinations, let alone of Bart's poor neck.

You can place the blame squarely on the male Simpsons. Amid the tempestuous cauldron that they lovingly call home, the female members of the family usually manage to keep their wits about them. Immersed in situations that would rattle even the steeliest nerves, they typically offer the calm voice of reason. Even the continuous chomp-chomp of Maggie's pacifier offers a sedate mantra that seems to put matters in perspective.

What could explain the profound differences between the male and the female Simpsons? Is it purely a matter of differing expectations and environmental conditions—in Bart's case, for example, a reduced supply of oxygen through his trachea that occurs at regular intervals—or could there be a genetic component? In the episode "Lisa the Simpson," this question comes to the fore when Lisa wonders if simply being in her family dooms her to daftness and finds considerable relief when she learns that her gender could spare her.

The episode starts off with Lisa fearing that she is losing her intellectual gifts, such as solving math problems and belting out jazz pieces on her saxophone. Lisa prides herself on her intellect—demonstrated, for instance, in another episode where she attends a Halloween costume contest dressed as Albert Einstein. She clearly doesn't want to grow up and be just like the rest of her family. Homer and Bart often embarrass her with their childish antics, Marge is not fully realized, and Lisa sincerely hopes that her sharp mind will propel her to better things. But what if her powers of thought sputter before they convey her to her rightful position in life, and she ends up just like the other family members?

Lisa's anxieties skyrocket when Grandpa tells her about the "Simpson gene," a genetic predisposition to mental decline that kicks in during mid-childhood. As young children, Grandpa explains, Simpsons act perfectly normal. Slowly, however, the Simpson gene triggers deterioration of the brain, leading to lives of utter mediocrity or worse. Naturally, Lisa is petrified that the same thing will happen to her.

In an attempt to dispel Grandpa's theory and cheer Lisa up,

Homer invites a number of their relatives over. He asks them to describe what they do for a living, hoping the reports will impress her. Some of the male Simpsons speak first and, to Lisa's horror, turn out to be failures. Her great-uncle Chet has bungled running a shrimp firm. Her second cousin Stanley just hangs out at the airport and shoots birds. Another runs in front of cars to collect insurance money. None of these men give Lisa much hope.

Fortunately, several Simpson women chime in with glowing accounts of successful careers. One of them, the highly articulate Dr. Simpson, explain that the faulty Simpson gene is carried on the Y chromosome and passed down only from male to male. Lisa realizes that it's just the Simpson men who are doomed; the women are all fine.

Not only does this revelation mean that Lisa will grow up normal, it also implies that any children she has would be safe, too. But for Bart and other male family members having kids would be risky. This genetic roulette is the exact opposite of baseball—if you strike out, you get a Homer.

It is an interesting theory, but could a single gene create such an intellectual disparity between women and men in a family? Intelligence is a complex issue, with smartness and success due to a variety of factors, environmental as well as genetic, many of which are not fully understood. Indeed such complexity is borne out in other episodes of the series, in which the male/female differences among Simpson family members are not so clear-cut. For example, in the episode "Oh Brother, Where Art Thou?" Homer meets his long-lost half-brother, Herb, who turns out to be wealthy and extremely successful. In "The Regina Monologues," Homer travels to England and encounters his long-lost half-sister, Abbie, who appears remarkably similar to him in voice, appearance, and seeming brightness. So on the face of it, Homer-like characteristics couldn't be solely a male thing; there must be other factors.

Moreover, as mentioned in the introduction, at least part of Homer's difficulties stems from a crayon wedged in his brain since he was a kid. Childhood traumas can in some cases cause

impairment that extends into adulthood. Even without a specific incident, an overall environment hostile to learning could have profoundly negative repercussions throughout someone's life.

Children have an extraordinary capacity to adapt to whatever environment they are born into. The child who thrives in a nurturing, stimulating household might have faltered if born into a dreary, uncaring situation instead. Modeling themselves on their family members and friends, children often take on the attitudes and cultural norms of those around them. If a society radically changes its values—for example, renouncing violence after an age of militarism or becoming open and democratic after an era of totalitarianism—it's remarkable how quickly the bulk of its youth start to echo the new views. Thus environment and culture play tremendous roles in shaping the patterns of life.

Because of the profound influence of environmental factors, it's tempting to think that every child has unlimited potential to succeed in any area. Yet we must also recognize a genetic heritage that influences the pace of human development and the ultimate physical and mental limitations of individuals. No typical ten-year-old, no matter how extensively trained, could develop the strength to lift 400-pound weights or memorize all the names in the Chicago phone book. It would be foolish to expect that any kid practicing an instrument for ten hours each day could mimic the feats of Mozart or even develop enough proficiency to join a professional orchestra. Potential Olympic athletes must be identified at a very young age, not just for their abilities at the time, but also for their likely inherent potential.

The body's genome, or full set of genes, constitutes the codebook for how the body develops and functions. Each gene encodes a particular protein that typically serves a biological role, from the collagen in the skin to the muscle fibers in the heart. The two copies each of approximately 33,000 genes in the human body are arranged along 23 pairs of chromosomes. One copy of each gene comes from the mother and the other comes from the father, guaranteeing that everyone has a mixture of parental attributes.

Genes come in different sequence variations, called alleles. Each allele creates a difference in the constitution of the protein that a given gene encodes. For example, different alleles for the genes linked with eye color correspond to distinctive pigment proteins that in tandem could lead to variations in this trait. The specific pattern of genes is called the genotype. This should be distinguished from the phenotype, specifically how that pattern manifests itself as actual physical traits. Many different genetic patterns could end up producing the same trait—meaning that a range of genotypes could lead to the same phenotype. While phenotypes are often observed qualities, such as hair texture or whether or not someone can curl their tongue, determining a genotype generally requires genetic sequencing (mapping out the pattern of genes).

If chromosomes are the chapters of the body's encoding, and genes are the instructional pages with recipes for each protein, the specific sequence of bases on the helical, double-stranded molecules called deoxyribonucleic acid (DNA) constitutes the detailed language for these instructions. There are four different "letters" in the DNA "alphabet": the bases adenine, thymine, cytosine, and guanine, known as A, T, C, and G. Each base links with a partner on the opposite strand of the DNA: A with T and C with G. The particular arrangement of these bases produces the directions for manufacturing a multitude of different proteins.

Genes cannot synthesize proteins directly, however. Through a process called transcription, the coiled double helix of DNA creates single-stranded molecules called ribonucleic acid (RNA), which carry similar information but serve a different purpose. RNA differs from DNA in several ways, including its number of strands and the presence of the base uracil instead of thymine. One type of RNA, called messenger RNA (mRNA), forms a kind of protein assembly plant. Each set of three bases, called a codon, produces a specific type of amino acid. The particular chain of amino acids created in this process yields a certain type of protein.

Because cells in the human body carry (except for errors) identical versions of DNA, that cannot be the full story. When embryos

develop in the womb, cells divide and differentiate, expressing their genetic content in different ways. Consequently, soon after conception, after enough divisions have taken place, cells start to specialize into skin cells, nerve cells, muscle cells, and so forth. The cell's relative position in the developing embryo seems to play an important part in this. The process of differentiation has long been one of the greatest mysteries in biology and is currently a vital topic of study.

The governing factor in heredity is the fact that chromosomes come in pairs—one set of genetic contributions from each parent. A given gene could appear in the form of either different or similar alleles, meaning there could be one or two copies of each allele. Alleles may be either dominant or recessive, depending on their biochemical properties. If an allele is dominant, then even if there is only one copy, the trait associated with that allele expresses itself and becomes part of the phenotype. For a recessive allele, in contrast, two copies must be present for that trait to appear. These rules were discovered by the nineteenth-century Czech botanist Gregor Mendel, who performed extensive studies of pea plant characteristics. He found, for instance, that tall alleles always dominated over short ones, meaning that tall plants bred with either tall or short plants always produced tall offspring.

Some inherited characteristics are specific to sex and manifest themselves differently for female and male offspring. The twenty-third pair of chromosomes, known as the sex chromosomes, is composed of two varieties, X and Y. Women almost always have an XX pair and men almost always have XY. (There are some rare conditions with other combinations.) The X chromosome is far bigger and has many more genes than the Y. With approximately 1,100 genes, consisting of more than 150 million base pairs, the X chromosome constitutes about 5 percent of the total number of human genes. Contrast that with the Y chromosome, which has only 78 genes. In recent years, these genes have been fully mapped out by the researchers Richard Wilson and David Page of Washington University in St. Louis. Wilson and Page noted that the genes in the

Y chromosome are mainly centered around the functioning of male reproduction—formation of the testes, sperm production, and so forth. Because these few genes are so important for the propagation of the species, the Y chromosome has evolved with multiple backup copies of the set. This duplication provides an assurance that even if one group of male reproduction genes is faulty, another set could express itself instead.

Hence, at least in terms of the Y chromosome, redundancy seems to be a critical male trait. That is to say that repetition, in genetics, is an important aspect of maleness. In other words, men, at least with regard to the Y chromosome's genes, often repeat themselves. Or how else could I put this. . . ?

Now that the genetic profile of the Y chromosome is well known, it does not appear to contain any gene that directly affects intelligence and common sense (unless you count teenage distractions due to the hormones of puberty). Thus the Simpson gene couldn't be found on the Y chromosome, and it couldn't be linked only to men. Alas, if such a gene existed, it could not be passed down exclusively from male to male, and therefore Lisa would have no firm guarantees of escaping its effect.

It's possible instead that such a gene could be on the X chromosome, a situation called sex-linked. Ironically, a sex-linked trait, though associated with an X chromosome gene, would appear more often in men if the causal allele happens to be recessive. That's because for women there's a choice between alleles from two different X chromosomes, but for men there's only one possibility. Hence, recessive alleles on a male's X chromosome are generally expressed.

A son receives his X chromosome exclusively from his mother. Therefore, if he inherits a sex-linked trait, it must have stemmed from the maternal side. Any sex-linked traits Bart has acquired, for example, would have been from Marge's genetic contribution, not Homer's. Similarly, Homer's male-pattern baldness, a sex-linked trait, could be chalked up to a recessive gene passed down from his mother, Mona, rather than his father, Abe.

There is one known sex-linked trait connected with aspects of intelligence—a hereditary condition called fragile X syndrome, so named because of a noticeable gap or fragile region in the X chromosome. This syndrome is due to changes to a gene called FMR1 that preclude it from producing a protein called FMRP (fragile X mental retardation protein). A particular triple sequence of bases on the FMR1 gene—cytosine-guanine-guanine (CGG)—is normally repeated about thirty times. For some individuals, an alteration occurs called a premutation that significantly increases the number of repetitions of that triplet up to two hundred times. Some researchers believe premutation of FMR1 could lead to subtle deficits in the intellectual or behavioral areas. If someone within a premutated version of FMR1 has children, her offspring have an increased chance of acquiring that gene in the fully mutated form. In that version, the CGG sequence is repeated more than two hundred times, usually triggering a process that prevents the production of FMRP and leads to fragile X syndrome. Fragile X syndrome has been associated with a number of effects, including cognitive and learning disabilities as well as alterations in physical appearance that emerge during adulthood. Aside from Down syndrome, an unrelated chromosomal disorder, scientists believe that fragile X syndrome is the leading genetic cause of mental impairment. Because it is sex-linked, fragile X syndrome affects many more men than women.

Not all inherited characteristics that affect males and females differently are sex-linked traits. Sometimes genes located on autosomes (nonsex chromosomes) respond differently to male and female biochemistry and produce distinct traits. For such a situation, these traits are called sex-influenced. Hence it is possible that a Simpson gene could be sex-influenced, rather than sex-linked. In that case, both Bart and Lisa could have inherited it from Homer, yet perhaps their dissimilar biochemistries caused it to respond in different ways.

Intelligence represents a very complex set of abilities that differs greatly from individual to individual. Because of varying definitions,

researchers don't agree even on all the components of intelligence, let alone exactly which genes control it. It is also unclear how much depends on nature or nurture. Certain conditions that bear upon cognitive abilities, such as fragile X, have been mapped out, yet genetic research has a long way to go before being able to explain why family members, such as the Simpsons, act in such divergent ways.

Life has many mysteries, and the precise set of factors influencing Homer's erratic behavior appears to be one of them. He is a riddle wrapped in a mystery packed into stretchy blue trousers. Even the Human Genome Project could not unravel why Homer sapiens (as perhaps he could be classified) often operates with such bizarre motivations. How could we explain, for instance, why Homer would attempt to market a radiation-produced hybrid of tomatoes and tobacco?