TWEAKING THE GENETICS OF BEHAVIOR

How might new advances in behavioral genetics affect you and your children? A fictional couple plays design-a-baby. **By Dean Hamer**

SYD AND KAYLA had wanted to be parents for a long time, so when they sat down at their computer to enter the specifications for their new baby, they didn't hesitate. They logged on to SEED (Society's Ethical Engineering Department's Web site) and eagerly began the task of entering their decisions. Because Syd and Kayla were both women, they were going to clone a baby, and because Syd was the better-looking of the two, they had chosen to start with her genes. The child, a girl, would have Syd's comely features and lean build. But thanks to a technique called homologous gene replacement, she would also have the genes for Kayla's coloring and fine set of teeth cut-and-pasted into Syd's DNA. Syd and Kayla chose an adult height for their daughter of six feet—knowing that tall, thin women still seemed to have an advantage, even in the year 2250.

Now came the tough part: selecting the child's personality and temperament. Fortunately, Kayla was an expert in human behavioral genetics; indeed, she was in the midst of writing a history of the subject from the turn of the millennium for *Scientific Terran* (formerly known as *Scientific American*). Kayla's grasp of the crucial yet limited role of genetics in determining human behavior gave her a realistic view of what designing a baby was all about. The fact was, raising children wasn't all that different than it had been 250 years ago. Kayla knew that despite her choice of genes, a good home and the best education, a lot was left to pure chance. Experience and environment would richly texture her daughter's personality, and much of that life history would be a matter of serendipity.

Nevertheless, there were certain qualities Syd and Kayla could control to varying degrees. Just as medical advances in the 20th century had wiped out many deadly diseases, genetic advances in the 21st century had eradicated many forms of psychosis, addictions and just plain unpleasant behaviors. For Kayla, deciding to eliminate as many as possible of the disagreeable surprises that might be lurking in Syd's genes was easy. Targeted intervention seemed far less of a crapshoot than the old approach of meet, mate and procreate—talk about genetic experimentation! But she had to admit that the basis for some behaviors was not yet fully understood. In truth, behavior prediction through genetics remained as much art as science.

Figuring out the human genome sequence—determining the exact order of the more than six billion DNA bases that make up and separate the tens of thousands of genes in every human—had been accomplished early in the 21st century. (The project was actually completed sooner than the government had expected, as a result of the spontaneous collaboration of several major biotech firms, which snapped up patents on every gene they could find.) Enumerating all the genes and learning the mechanics of the proteins they encode took another 20 years after that. But deciphering the cellular and developmental functions of these proteins had taken until the turn of the 22nd century to complete. And scientists were still struggling to fathom how the trillions of possible gene combinations work together to influence the entire range of human behavior. Syd and Kayla could calculate the probability that their child would have a particular behavioral peccadillo—a tendency to oversleep, a taste for strange foods, a penchant for taking risks such as skinny-

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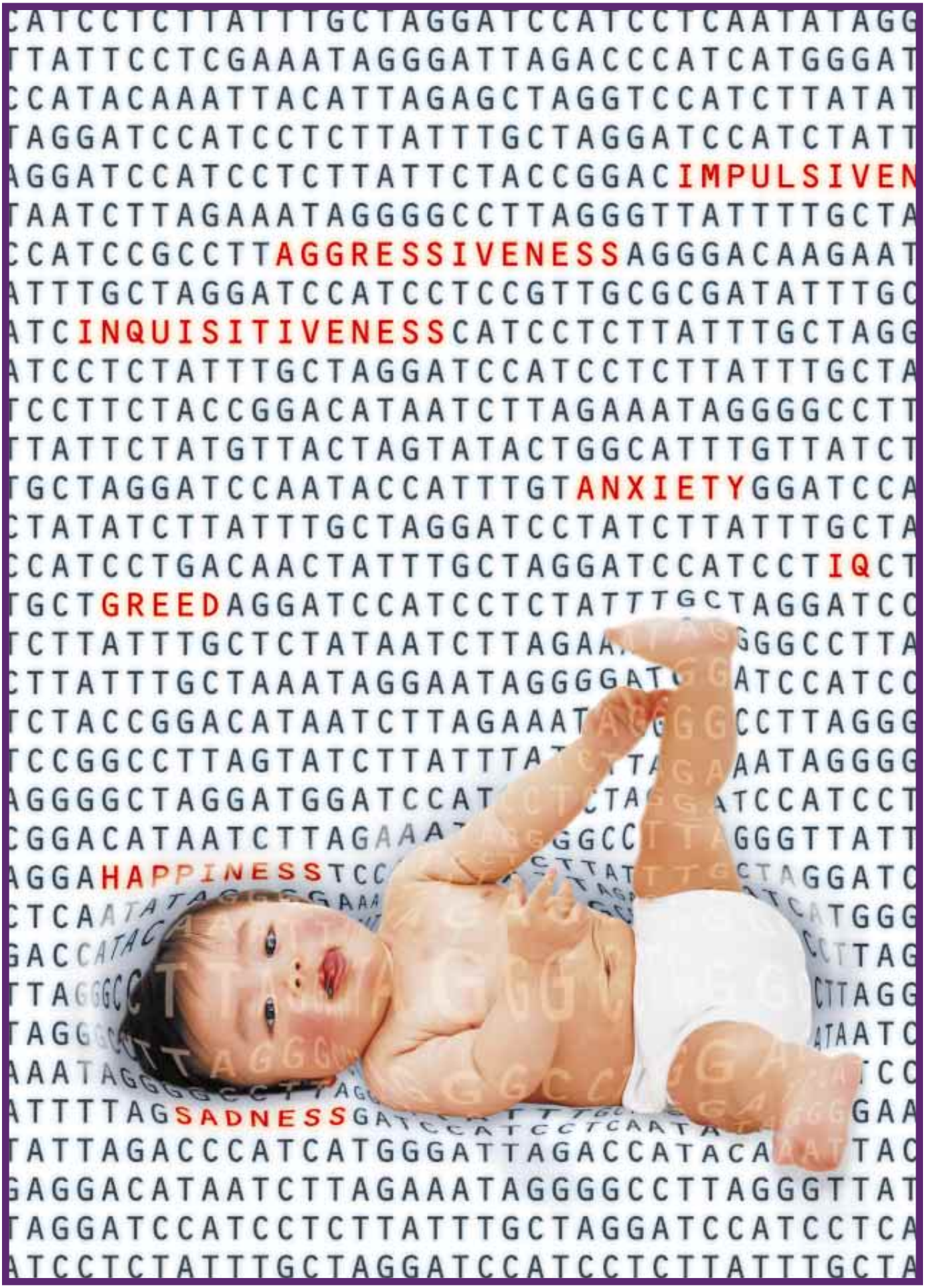
Geneticists are deciphering the molecular underpinning of dozens of behavioral traits, from aggressiveness to shyness. In the future, couples who want children might be able to decide on more than just the baby's sex.



dipping—but they could not precisely predict her behavior at too detailed a level. As a scientist, Kayla could live with this uncertainty, but the whole undertaking had Syd a little worried.

One thing scientists did know by 2250 was that more than half of a person's genes are involved in shaping behavior. This wasn't surprising, because it had been understood even in the 20th century that more than 50 percent of genes are copied into messenger RNA—turned on, as it were—in the brain. At first, the researchers had tried to determine what all these brain genes did using an old-fashioned "one gene, one behavior" model, but they didn't get very far. The link between brain function and behavior turned out to be far more intricate.

The first breakthrough came when scientists determined the sequence of all the genes of humankind's closest relative, the chimpanzee. As far back as the 20th century, scientists had known that these primates are almost genetically identical to people, with only a 1 percent disparity between the two. By exploring the specific genetic differences, scientists of the 21st century had pinpointed the regions of the human genetic complement responsible for the most human traits, such as cognition, intelligence and consciousness. Geneticists had long suspected that when it came to these characteristics, people simply had different genes than other primates. They were wrong. Most of the variations were found not in the DNA sequences that carry the instructions for building proteins but rather in the snippets of DNA that control whether individual genes are read out. Remarkably, being human was determined more by where, when and how much protein the genes make than by the types of proteins they produce. Humans were even closer to their primate cousins than anyone had guessed. Kayla thought this was beautiful; Syd told her to please stop comparing their daughter to monkeys.

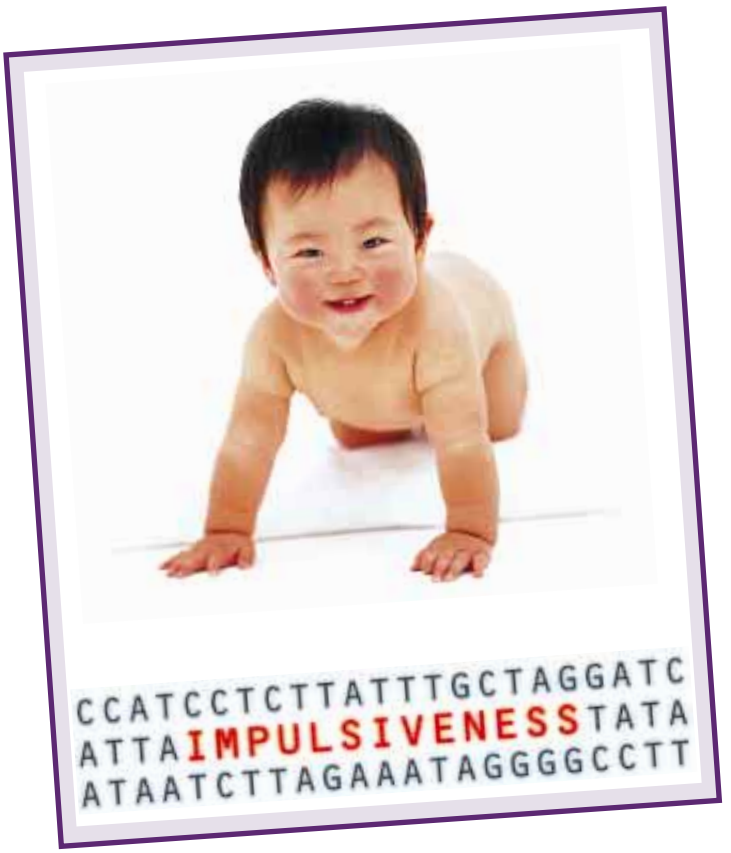
The next big advance in understanding and manipulating the genetics of behavior was helped along by another animal—humanity's best friend, the dog. People had been breeding dogs for thousands of years to emphasize useful traits such as speed, vigilance and an uncontrollable desire to herd things like sheep. Dogs had become tightly inbred; the purebred strains were much more identical genetically than were humans, so genetic mapping in dogs was much easier than in humans. Scientists hit pay dirt in the 21st century, when they were able to identify and then insert a cluster of behavioral genes from a Siberian husky into a greyhound—making a new breed, the greyhusk, which combined the speed of a greyhound with a sled dog's capability for teamwork and harmony. (Several harrowing Iditarod races later, humans finally learned how to cope with the "improvement.")

The information and techniques gleaned from studying chimps and dogs laid the groundwork for a revolution in human behavioral genetics that Syd and Kayla were about to tap. Much of the early work in the 22nd century had focused on intelligence. With bright young women already selling their eggs for tens of thousands of dollars in the late 1990s, there had been no question of a vast and lucrative market for "smart" genes. And researchers quickly confirmed what some scientists had long suspected: intelligence is one of the most heritable human traits.

Studies of twins—Twins!?! Better double-check that part of the form now, Kayla thought—conducted during the 20th century

had suggested that genes are responsible for perhaps half the variation in the old-style IQ test scores. (The genetic contribution to IQ appeared to be stronger in older people, whereas younger ones seemed more malleable.) But in the past 250 years scientists had found that the genetic architecture of intelligence was incredibly baroque. They had identified more than 10,000 different genes that contribute to intelligence. And although there were clearly many simple ways to lower IQ drastically, no change in any individual gene had been found to raise it by more than a point—and most added much less than that.

Thousands of the genes involved in intelligence had turned out to code for housekeeping enzymes—ho-hum proteins involved in the everyday maintenance of cellular metabolism throughout the entire body, not just the brain. Because the brain is so delicate, minor genetic changes that throw metabolism even the slightest bit out of kilter alter its function. Although researchers did discover some genes that were specific for human intelligence, these showed remarkably little variation from one person to the next. All people, from the smartest to the dumbest, had these genes. It was the fine-tuning, not the basic construction of the brain, that was controlled by genetic variation. This news had spelled ruin for many a gene-tech start-up company; so far there wasn't much anyone could do to improve intelligence genetically. The real advances had come in the form of cybernetic devices that were implanted within the brain to enhance its function. If Syd and Kayla wanted their child to be able to recite an entire encyclopedia, they would have to put in a request with the neuroimplant experts, not the geneticists; Kayla made herself a note to do just that.



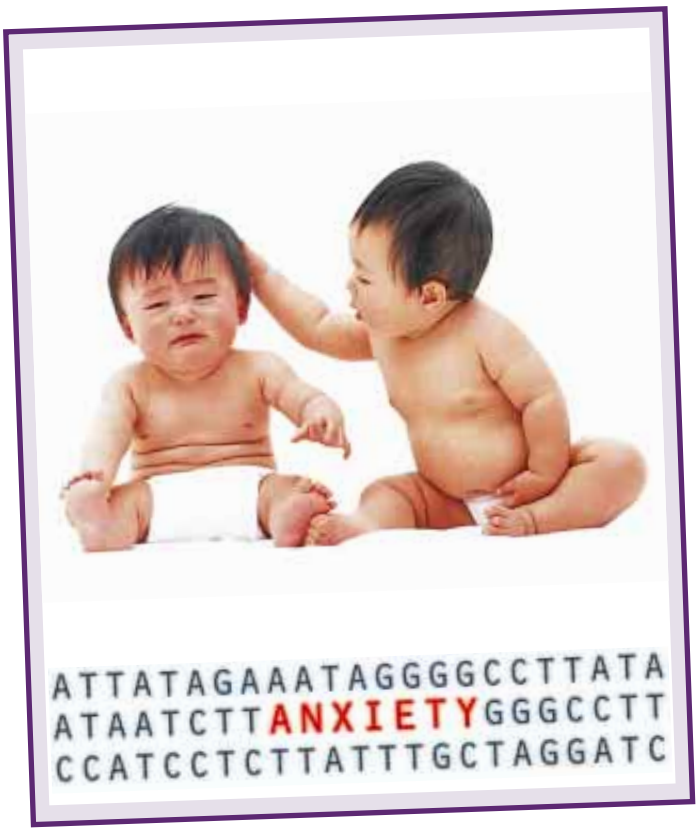
Undaunted by their defeat in the arena of human intelligence, the gene brokers had moved on to other traits and, by the time Syd and Kayla were placing their order, had discovered other aspects of human behavior that were more amenable to genetic manipulation. Predictably, this development caused much hand-wringing among those concerned about whether this power would be used for good or for evil. By the year 2150, as the technology for gene transfer improved and the possibility of eugenics turned into a reality, world opinion reached critical mass. SEED, an organization with members from every part of the world, was formed to oversee genetic selection for each individual born or cloned. The fees were a bit exorbitant, but because they were used to fund new research, Kayla didn't mind paying.

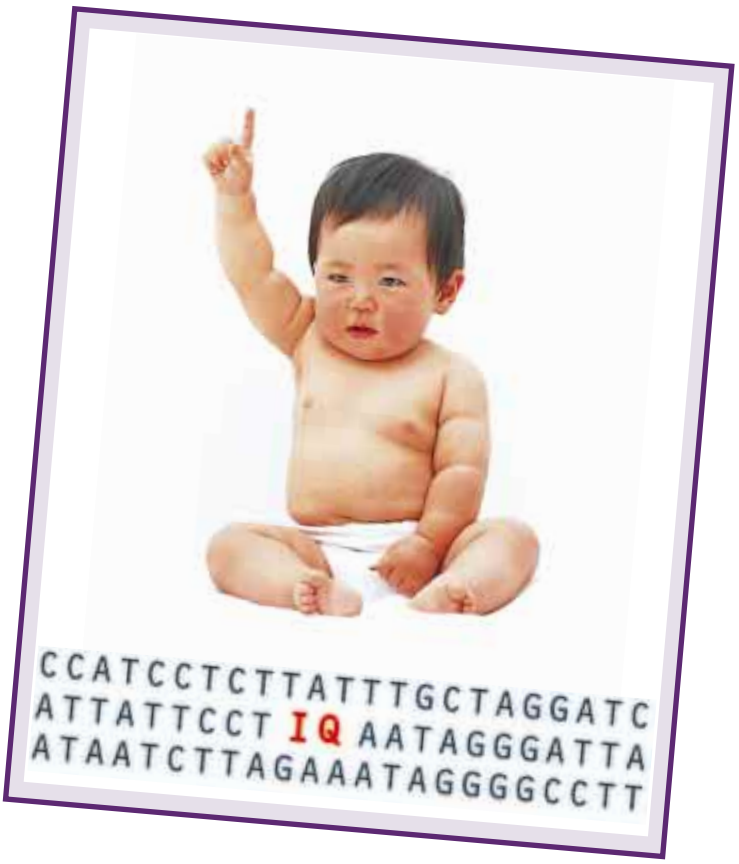
Altruism and happiness were two of the traits that Syd and Kayla were allowed to select for their new baby. As predicted by sociobiologists 250 years previously, altruism was as much in the genes as in upbringing. Unexpectedly, almost all the contributory genes were pleiotropic, meaning that they influenced more than one trait. The same cluster of genes that controls charity, for example, also turned out to have an effect on greed. Syd and Kayla pondered the choices before them, which ranged from the altruism level of Mother Teresa to the most cutthroat CEO. Typically Syd was leaning toward sainthood; Kayla argued for an entrepreneur. In the end, they chose a level midway between, hoping for the perfect mix of benevolence and competitive edge.

There was an even wider range of choices available for happiness, one of the most popular engineered traits. In 2250 most people were even more interested in leading a fulfilled, happy life than in being "accomplished." The gene peddlers' research had con-

firmed what some scientists in the 1990s had already suspected: happiness was actually affected by two independent physiological mechanisms: one that generated negative emotions and another that led to a positive outlook. Back then, twin studies had shown that genes were probably responsible for about half of a person's tendency to happiness and feelings of well-being; by the time Syd and Kayla were making their decisions, more than 700 such genes had been identified.

Some of the genes coded for enzymes that synthesize and degrade a dozen or so neurotransmitters, chemicals that shuttle signals around in the brain. Others made hundreds of different receptors, proteins on the surfaces of cells that receive chemical signals





from the outside. And then of course there were the genes encoding proteins that interpret the messages within the cells. By fiddling with these genes it was now possible to increase happiness so that, for the most part, people were able to shrug off life's daily annoyances. The words "worrywart," "hypersensitive" and "jerk" weren't used much anymore. Syd and Kayla, however, did not want to set their child's happiness rheostat too high. They wanted her to be able to feel real emotions. If there was a death, they wanted her to mourn the loss; if there was a birth, she should rejoice. Deciding how happy their child would be had been the hardest question they had asked themselves.

Satisfied that their little girl would ride the ups and downs of her life's roller coaster with relative equanimity, Syd and Kayla turned their attention to the more severe forms of mental illness. By now the genes underlying all the classic forms of psychosis had been identified, but this achievement had taken some time. For decades, researchers had searched for the genes responsible for "schizophrenia," a quaint 20th-century term for a mixed bag of brain disorders. They had made little progress until neurobiologists developed elaborate imaging assays to distinguish different subtypes of the disease by their unique neurochemical patterns. Now more than 20 different types of schizophrenia were recognized. Some were primarily genetic, but others were found to be triggered by environmental factors, such as microbes. Other mental disorders—including bipolar (manic-depressive) disease, obsessive-compulsive disorder and attention-deficit hyperactivity disorder—had also been found to have a rich mixture of genetic and environmental causes. Some of these, such as an alteration in a particular receptor in the brain for the neurotransmitter dopamine, had been suspected for centuries, but others, such as the chemical makeup of grilled meat, had come as a complete shock.

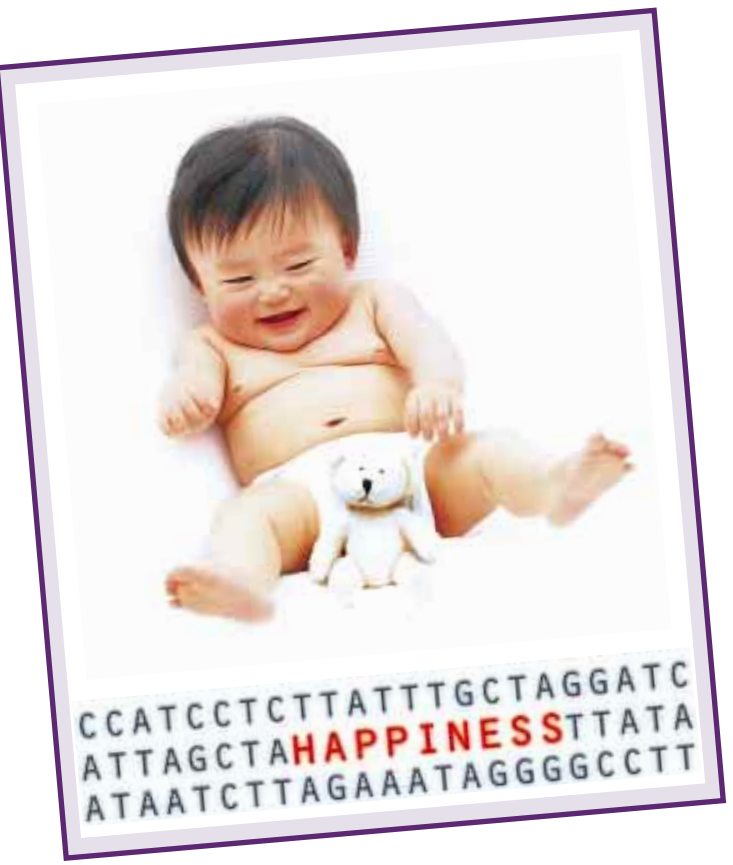
This news was disheartening to Syd. She had hoped to engineer away the possibility of mental illness altogether—that had seemed to be one of the upsides of this whole cloning business. But Kayla reassured her that the years of research had also paved the way for hundreds of different drugs, each specifically tailored to compensate for a particular type of genetic defect or environmental damage: what they couldn't eliminate they could almost certainly medicate. This was especially true of the trait that worried Syd the most. At first the couple had hesitated to use her genes at all because of a discouraging trend toward alcoholism in her family.

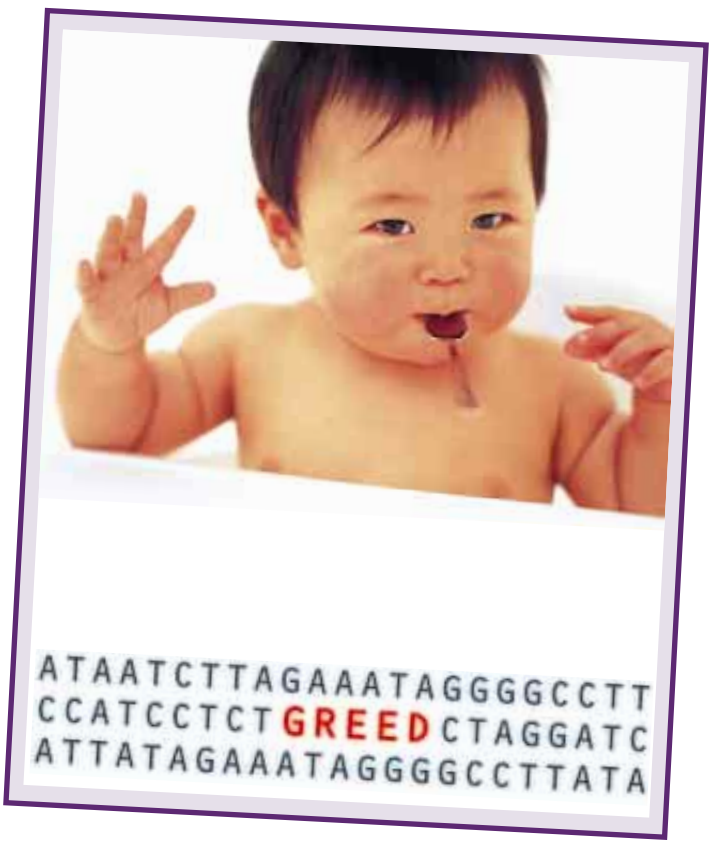
It was true that most of Syd's immediate relatives had been conceived in a dish and had had at least some remedial gene customization done. And each of them had been preapproved by

SEED, using Predicti-Chip technology that rapidly screened their genetic blueprint for thousands of potential defects. But Syd's was still a clan of tipplers. Even though scientists recognized centuries ago that alcoholism runs in families, it was only in the past few decades that they had finally identified a suite of genes that predicted with 50 percent accuracy the likelihood a person would become addicted. Although many of Syd's relatives had since been diagnosed with a familial susceptibility to alcohol, they still didn't always steer clear of the stuff, and most had developed the disease. No matter how badly the genetic deck was stacked against them, they refused to believe they could become alcoholics—that much hadn't changed since 2000.

aging had been identified. This made the final years of life far less distressing but had actually extended the average life span only 30 years; as people's biological clocks kept on ticking, their bodies and brains simply wore down by the time they got to be much over 100.

More recently, however, scientists at Methuselah Inc. had succeeded in identifying the genes that acted as the body's basic chronometer. Using genetic methods learned through centuries of tinkering with fruit flies and worms, it was now possible to more than double the average life span of a human to over 200 years. But for the first generation experiencing this longevity, it was a decidedly mixed blessing. Two hundred years was a long time to go on living. Three or four careers and six sets of grandchildren were simply too much. So Syd and Kayla settled on a genetic makeup that would allow their daughter to live for a nice, moderate 115 years.





Syd was relieved to see her own test results: they pretty much guaranteed that her daughter was not going to inherit a vulnerability to alcohol. The inheritance of alcoholism seemed to be attributable to random events during the wiring of the fetal brain. Nothing could be done about that yet, but fortunately an effective antialcoholism drug was now on the market. Soberitin worked by specifically blunting the brain's dopamine-dependent pleasure circuits that were susceptible to alcohol, so that a flute of champagne became no more pleasurable than a glass of water.

Syd and Kayla's little girl would be tall, thin, attractive, altruistic, reasonably happy, and free of alcohol addiction and mental illness. With a life like that, who wouldn't want to live forever? With that thought in mind, Syd and Kayla turned to the longevity section of their order form. By late in the 21st century, the genes for Alzheimer's disease, Parkinson's disease, cancer, heart disease, diabetes and essentially all other common disorders of

Their choices made, they submitted their application and waited for their confirmation number. The technicalities of the cloning would take place the next day, and then Syd and Kayla would confront a human decision that had not changed one iota in the new millennium—what on earth to name the baby.

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