



S C I E N C E

# WHAT MAKES YOU WHO YOU ARE

Which is stronger—nature or nurture? The latest science says genes and your experience interact for your whole life

By MATT RIDLEY

**T**HE PERENNIAL DEBATE ABOUT NATURE AND NURTURE—WHICH IS the more potent shaper of the human essence?—is perennially rekindled. It flared up again in the *London Observer* of Feb. 11, 2001. REVEALED: THE SECRET OF HUMAN BEHAVIOR, read the banner headline. ENVIRONMENT, NOT GENES, KEY TO OUR ACTS. The source of the story was Craig Venter, the self-made man of genes who had built a private company to read the full sequence of the human genome in competition with an international consortium funded by taxes and charities. That sequence—a string of 3 billion letters, composed in a four-letter alphabet, containing the complete recipe for building and running a human body—was to be published the very next day (the competition ended in an arranged tie). The first analysis of it had revealed that there were just 30,000 genes in it, not the 100,000 that many had been estimating until a few months before.

Illustrations for TIME by Tavis Coburn



Details had already been circulated to journalists under embargo. But Venter, by speaking to a reporter at a biotechnology conference in France on Feb. 9, had effectively broken the embargo. Not for the first time in the increasingly bitter rivalry over the genome project, Venter's version of the story would hit the headlines before his rivals'. "We simply do not have enough genes for this idea of biological determinism to be right," Venter told the *Observer*. "The wonderful diversity of the human species is not hard-wired in our genetic code. Our environments are critical."

In truth, the number of human genes changed nothing. Venter's remarks concealed two whopping nonsequiturs: that fewer genes implied more environmental influences and that 30,000 genes were too few to explain human nature, whereas 100,000 would have been enough. As one scientist put it to me a few weeks later, just 33 genes, each coming in two varieties (on or off), would be enough to make every human being in the world unique. There are more than 10 billion combinations that could come from flipping a coin 33 times, so 30,000 does not seem such a small number after all. Besides, if fewer genes meant more free will, fruit flies would be freer than we are, bacteria freer still and viruses the John Stuart Mill of biology.

Fortunately, there was no need to reassure the population with such sophisticated calculations. People did not weep at the humiliating news that our genome has only about twice as many genes as a worm's. Nothing had been hung on the number 100,000, which was just a bad guess.

But the human genome project—and the decades of research that preceded it—did force a much more nuanced understanding of how genes work. In the early days, scientists detailed how genes encode the various proteins that make up the cells in our bodies. Their more sophisticated and ultimately more satisfying discovery—that gene expression can be modified by experience—has been gradually emerging since the 1980s. Only now is it dawning on scientists what a big and general idea it implies: that learning itself consists of nothing more than switching genes on and off. **The more we lift the lid on the genome, the more vulnerable to experience genes appear to be.**

This is not some namby-pamby, middle-

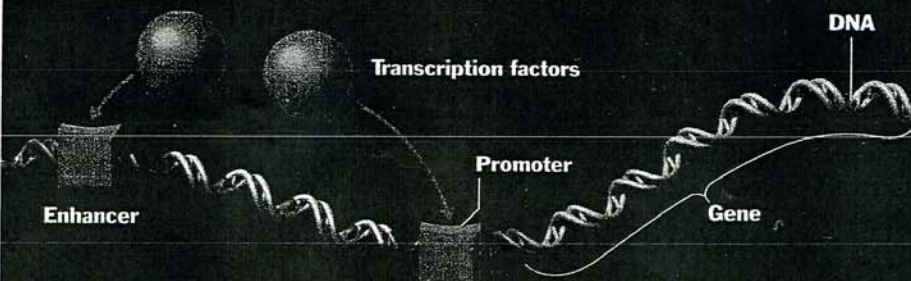
*Matt Ridley is an Oxford-trained zoologist and science writer whose latest book is Nature via Nurture*

# NURTURING NATURE

**Genes are not static blueprints that dictate our destiny. How they are expressed—where and when they are turned on or off and for how long—is affected by changes in the womb, by the environment and by other factors**

## How genes get switched on ...

**1** Most genes have a switch, called a promoter, that controls how, when and even if the gene becomes active. (Other regulatory elements, called enhancers, also play a role.) The promoter and enhancers are able to do their jobs only after so-called transcription factors attach to them



**2** Once transcription factors are attached, other enzymes are able to make an RNA copy of the gene, the first step in the long process of building a protein needed by the cell



Sources: Cooduvalli S. Shashikant, Pennsylvania State University and other associates of Frank Ruddle, Yale University; Anne Burke, Wesleyan University; M.J. Cohn and C. Tickle, University of Reading, Britain

Photos: TED THAI FOR TIME; TIME Graphic by Joe Lertola

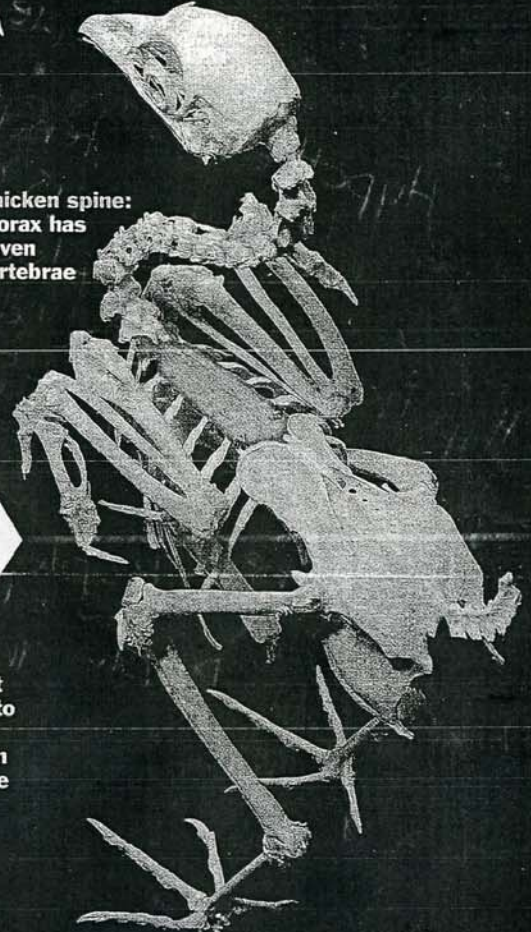
## ... and contribute to evolution

**3** Slight alterations in the promoters can lead to dramatic changes in when and where genes are expressed. Various environmental factors can influence how easily a transcription factor binds to the promoter. Consider the example of the *Hoxc8* gene, which is responsible for determining the location of the thorax, which includes the chest area, of an animal. Rats, chickens and pythons seem to have slightly different promoters that allow their respective *Hoxc8* genes to be turned on in slightly different configurations during development. Extensive activation produces an animal that's almost all thorax—like the python. Limited activation gives the chicken a short thorax. And the expression of the *Hoxc8* gene in the rat, with its medium-size thorax is, as you might expect, intermediate

Rat spine:  
thorax has 13 vertebrae

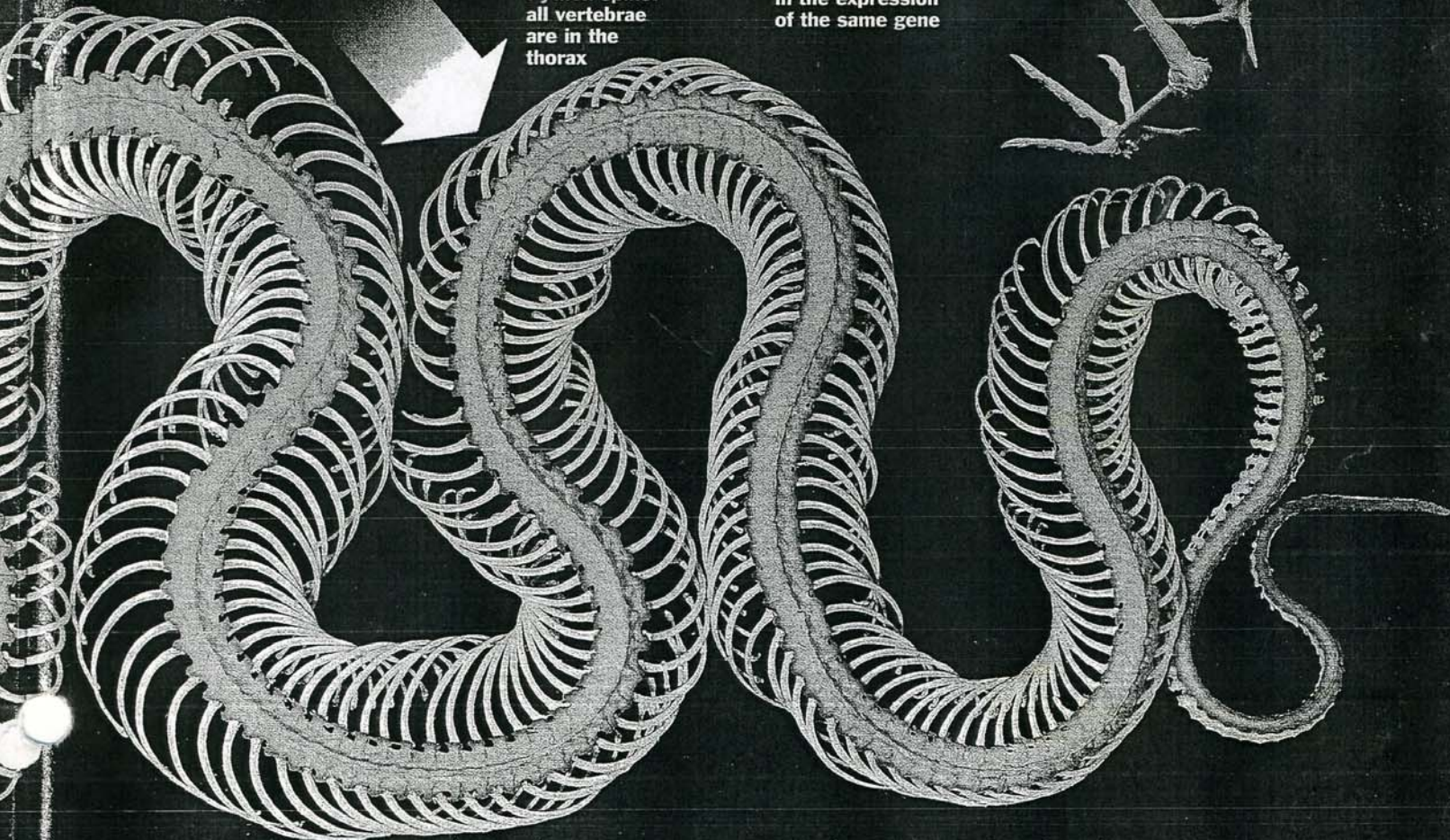


Chicken spine:  
thorax has  
seven  
vertebrae

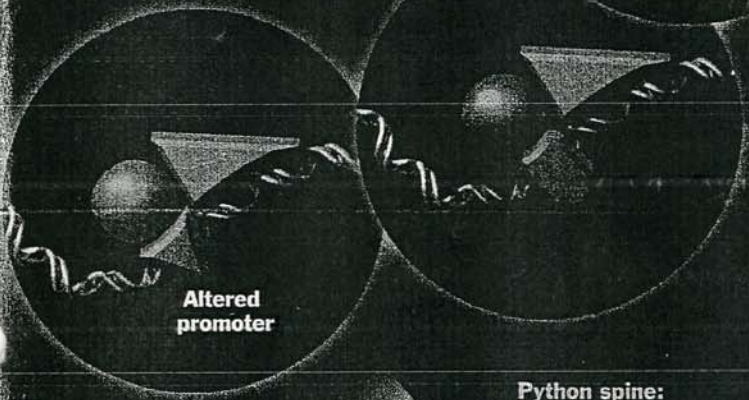


Slightly different  
promoters lead to  
big differences  
in the expression  
of the same gene

Python spine:  
all vertebrae  
are in the  
thorax



Altered  
promoter



of-the-road compromise. This is a new understanding of the fundamental building blocks of life based on the discovery that genes are not immutable things handed down from our parents like Moses' stone tablets but are active participants in our lives, designed to take their cues from everything that happens to us from the moment of our conception.

For the time being, this new awareness has taken its strongest hold among scientists, changing how they think about everything from the way bodies develop in the womb to how new species emerge to the inevitability of homosexuality in some people. (More on all this later.) But eventually, as the general population becomes more attuned to this interdependent view, changes may well occur in areas as diverse as education, medicine, law and religion. Dieters may learn precisely which combination of fats, carbohydrates and proteins has the greatest effect on their individual waistlines. Theologians may develop a whole new theory of free will based on the observation that learning expands our capacity to choose our own path. As was true of Copernicus's observation 500 years ago that the earth orbits the sun, there is no telling how far the repercussions of this new scientific paradigm may extend.

To appreciate what has happened, you will have to abandon cherished notions and open your mind. You will have to enter a world in which your genes are not puppet masters pulling the strings of your behavior but puppets at the mercy of your behavior, in which instinct is not the opposite of learning, **environmental influences are often less reversible than genetic ones, and nature is designed for nurture.**

**Fear of snakes, for instance, is the most common human phobia, and it makes good evolutionary sense for it to be instinctive. Learning to fear snakes the hard way would be dangerous. Yet experiments with monkeys reveal that their fear of snakes (and probably ours) must still be acquired by watching another individual react with fear to a snake. It turns out that it is easy to teach monkeys to fear snakes but very difficult to teach them to fear flowers. What we inherit is not a fear of snakes but a predisposition to learn a fear of snakes—a nature for a certain kind of nurture.**

## Early Puberty

Girls raised in **FATHERLESS HOUSEHOLDS** experience puberty earlier. Apparently, the change in timing is the reaction of a **STILL MYSTERIOUS** set of genes to their **ENVIRONMENT**. Scientists don't know how many **SETS OF GENES** act this way

Before we dive into some of the other scientific discoveries that have so thoroughly transformed the debate, it helps to understand how deeply entrenched in our intellectual history the false dichotomy of nature vs. nurture became. Whether human nature is born or made is an ancient conundrum discussed by Plato and Aristotle. Empiricist philosophers such as John Locke and David Hume argued that the human mind was formed by experience; nativists like Jean-Jacques Rousseau and Immanuel Kant held that there was

such a thing as immutable human nature.

It was Charles Darwin's eccentric mathematician cousin Francis Galton who in 1874 ignited the nature-nurture controversy in its present form and coined the very phrase (borrowing the alliteration from Shakespeare, who had lifted it from an Elizabethan schoolmaster named Richard Mulcaster). Galton asserted that human personalities were born, not made by experience. At the same time, the philosopher William James argued that human beings have more instincts than animals, not fewer.

In the first decades of the 20th century, nature held sway over nurture in most fields. In the wake of World War I, however, three men recaptured the social sciences for nurture: John B. Watson, who set out to show how the conditioned reflex, discovered by Ivan Pavlov, could explain human learning; Sigmund Freud, who sought to explain the influence of parents



and early experiences on young minds; and Franz Boas, who argued that the origin of ethnic differences lay with history, experience and circumstance, not physiology and psychology.

Galton's insistence on innate explanations of human abilities had led him to espouse eugenics, a term he coined. Eugenics was enthusiastically adopted by the Nazis to justify their campaign of mass murder against the disabled and the Jews. Tainted by this association, the idea of innate behavior was in full retreat for most of the middle years of the century. In 1958, however, two men began the counterattack on behalf of nature. Noam Chomsky, in his review of a book by the behaviorist B.F. Skinner, argued that it was impossible to learn human language by trial and error alone; human beings must come already equipped with an innate grammatical skill. Harry Harlow did a simple experiment that showed that a baby monkey prefers a soft, cloth model of a mother to a hard, wire-frame mother, even if the wire-frame mother provides it with all its milk; some preferences are innate.

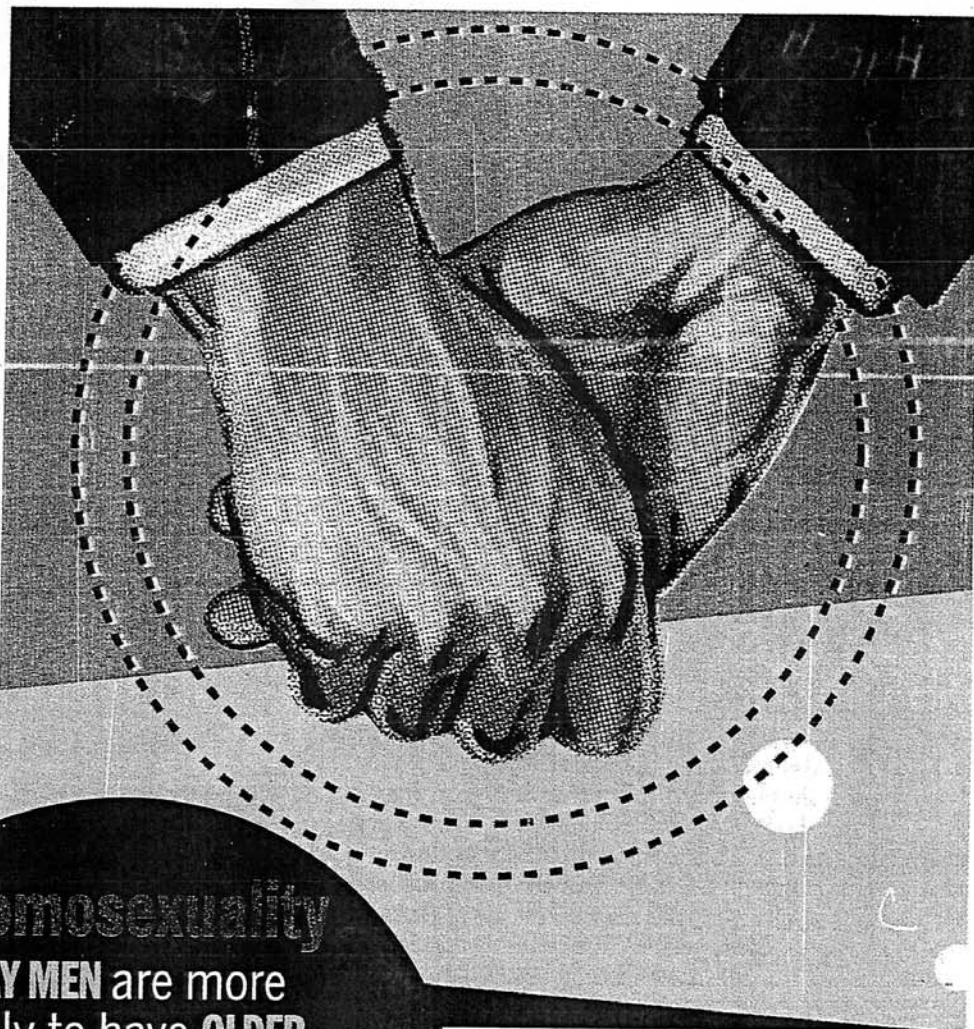
Fast-forward to the 1980s and one of the most stunning surprises to greet scientists when they first opened up animal genomes: fly geneticists found a small group of genes called the hox genes that seemed to set out the body plan of the fly during its early development—telling it roughly where to put the head, legs, wings and so on. But then colleagues studying mice found the same hox genes, in the same order, doing the same job in Mickey's world—telling the mouse where to put its various parts. And when scientists looked in our genome, they found hox genes there too.

Hox genes, like all genes, are

switched on and off in different parts of the body at different times. In this way, genes can have subtly different effects, depending on where, when and how they are switched on. The switches that control this process—stretches of DNA upstream of genes—are known as promoters.

Small changes in the promoter can have profound effects on the expression of a hox gene. For example, mice have short necks and long bodies; chickens have long necks and short bodies. If you count the vertebrae in the necks and thoraxes of mice and chickens, you will find

that a mouse has seven neck and 13 thoracic vertebrae, a chicken 14 and seven, respectively. The source of this difference lies in the promoter attached to HoxC8, a hox gene that helps shape the thorax of the body. The promoter is a 200-letter paragraph of DNA, and in the two species it differs by just a handful of letters. The effect is to alter the expression of the HoxC8 gene in the development of the chicken embryo. This means the chicken makes thoracic vertebrae in a different part of the body than the mouse. In the python, HoxC8 is expressed right from



**Homosexuality**  
**GAY MEN** are more likely to have **OLDER BROTHERS** than either gay women or heterosexual men. It may be that a **FIRST MALE FETUS** triggers an immune reaction in the mother, **ALTERING THE EXPRESSION** of key gender genes

the head and goes on being expressed for most of the body. So pythons are one long thorax; they have ribs all down the body.

To make grand changes in the body plan of animals, there is no need to invent new genes, just as there's no need to invent new words to write an original novel (unless your name is Joyce). All you need do is switch the same ones on and off in different patterns. Suddenly, here is a mechanism for creating large and small evolutionary changes from small genetic differences. Merely by adjusting the se-



ter our understanding of human nature. Take a look at four examples.

**LANGUAGE** Human beings differ from chimpanzees in having complex, grammatical language. But language does not spring fully formed from the brain; it must be learned from other language-speaking human beings. This capacity to learn is written into the human brain by genes that open and close a critical window during which learning takes place. One of those genes, FoxP2, has recently been discovered on human chromosome 7 by Anthony Monaco and his colleagues at the Wellcome Trust Centre for Human Genetics in Oxford. Just having the FoxP2 gene, though, is not enough. If a child is not exposed to a lot of spoken language during the critical learning period, he or she will always struggle with speech.

**LOVE** Some species of rodents, such as the prairie vole, form long pair bonds with their mates, as human beings do. Others, such as the montane vole, have only transitory liaisons, as do chimpanzees. The difference, according to Tom Insel and Larry Young at Emory University in Atlanta, lies in the promoter upstream of the oxytocin- and vasopressin-receptor genes. The insertion of an extra chunk of DNA text, usually about 460 letters long, into the promoter makes the animal more likely to bond with its mate. The extra text does not create love, but perhaps it creates the possibility of falling in love after the right experience.

**ANTISOCIAL BEHAVIOR** It has often been suggested that childhood maltreatment can

**Divorce**  
If a **FRATERNAL TWIN** gets divorced, there's a **30% CHANCE** that his or her twin will get divorced as well. If the twins are **IDENTICAL**, however, one sibling's divorce **BOOSTS THE ODDS** to **45%** that the other will split

Likewise, the development of a certain human behavior takes a certain time and occurs in a certain order, just as the cooking of a perfect soufflé requires not just the right ingredients but also the right amount of cooking and the right order of events.

How does this new view of genes al-

quence of a promoter or adding a new one, you could alter the expression of a gene.

In one sense, this is a bit depressing. It means that until scientists know how to find gene promoters in the vast text of the genome, they will not learn how the recipe for a chimpanzee differs from that for a person. But in another sense, it is also uplifting, for it reminds us more forcefully than ever of a simple truth that is all too often forgotten: bodies are not made, they grow. The genome is not a blueprint for constructing a body. It is a recipe for baking a body. You could say the chicken embryo is marinated for a shorter time in the HoxC8 sauce than the mouse embryo is.

## ANCIENT QUARREL

How much of who we are is learned or innate is an argument with a fruitful but fractious pedigree

### Nature

We may be destined to be bald, mourn our dead, seek mates, fear the dark



**IMMANUEL KANT**  
His philosophy sought a native morality in the mind



**FRANCIS GALTON**  
Math geek saw mental and physical traits as innate



**KONRAD LORENZ**  
Studied patterns of instinctive behavior in animals



**NOAM CHOMSKY**  
Argued that human beings are born with a capacity for grammar

### Nurture

But we can also learn to love tea, hate polkas, invent alphabets and tell lies



**JOHN LOCKE**  
Considered the mind of an infant to be a tabula rasa, or blank slate



**IVAN PAVLOV**  
Trained dogs to salivate at the sound of the dinner bell



**SIGMUND FREUD**  
Felt we are formed by mothers, fathers, sex, jokes and dreams



**FRANZ BOAS**  
Believed chance and environs are key to cultural variation

create an antisocial adult. New research by Terrie Moffitt of London's Kings College on a group of 442 New Zealand men who have been followed since birth suggests that this is true only for a genetic minority. Again, the difference lies in a promoter that alters the activity of a gene. Those with high-active monoamine oxidase A genes were virtually immune to the effects of mistreatment. Those with low-active genes were much more antisocial if maltreated, yet—if anything—slightly less antisocial if not maltreated. The low-active, mistreated men were responsible for four times their share of rapes, robberies and assaults. In other words, maltreatment is not enough; you must also have the low-active gene. And it is not enough to have the low-active gene; you must also be maltreated.

**HOMOSEXUALITY** Ray Blanchard at the University of Toronto has found that gay men are more likely than either lesbians or heterosexual men to have older brothers (but not older sisters). He has since confirmed this observation in 14 samples from many places. Something about occupying a womb that has held other boys occasionally results in reduced birth weight, a larger placenta and a greater probability of homosexuality. That something, Blanchard suspects, is an immune reaction in the mother, primed by the first male fetus, that grows stronger with each male pregnancy. Perhaps the immune response affects the expression of key genes during brain development in a way that boosts a boy's attraction to his own sex. Such an explanation would not hold true for all gay men, but it might provide important clues into the origins of both homosexuality and heterosexuality.

TO BE SURE, EARLIER SCIENTIFIC DISCOVERIES had hinted at the importance of this kind of interplay between heredity and environment. The most striking example is Pavlovian conditioning. When Pavlov announced his famous experiment a century ago this year, he had apparently discovered how the brain could be changed to acquire new knowledge of the world—in the case of his dogs, knowledge that a bell foretold the arrival of food. But now we know how the brain changes: by the



## Crime Families

**GENES** may influence the way people respond to a "crimogenic" **ENVIRONMENT**. How else to explain why the **BIOLOGICAL** children of criminal parents are more likely than their **ADOPTED** children to break the **LAW**?

real-time expression of 17 genes, known as the CREB genes. They must be switched on and off to alter connections among nerve cells in the brain and thus lay down a new long-term memory. These genes are at the mercy of our behavior, not the other way around. Memory is in the genes in the sense that it uses genes, not in the sense that you inherit memories.

In this new view, genes allow the human mind to learn, remember, imitate, imprint language, absorb culture and express instincts. Genes are not puppet masters or blueprints, nor are they just the carriers of heredity. They are active during life; they

switch one another on and off; they respond to the environment. They may direct the construction of the body and brain in the womb, but then almost at once, in response to experience, they set about dismantling and rebuilding what they have made. They are both the cause and the consequence of our actions.

Will this new vision of genes enable us to leave the nature-nurture argument behind, or are we doomed to reinvent it in every generation? Unlike what happened in previous eras, science is explaining in great detail precisely how genes and their environment—be it the womb, the classroom or pop culture—interact. So perhaps the pendulum swings of a now demonstrably false dichotomy may cease.

It may be in our nature, however, to seek simple, linear, cause-and-effect stories and not think in terms of circular causation, in which effects become their own causes. Perhaps the idea of nature via nurture, like the ideas of quantum mechanics and relativity, is just too counterintuitive for human minds. The urge to see ourselves in terms of nature versus nurture, like our instinctual ability to fear snakes, may be encoded in our genes. ■