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DNA referees

Scientists are just beginning to understand the effect lifestyle choices and other environmental factors have on altering gene behavior, a rapidly emerging field called epigenetics.

By Amber Dance, Special to the Los Angeles Times

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Your life story depends upon a combination of the DNA you're stuck with plus your environment, including all the little choices and events that happen over that lifetime.

But in recent years, researchers have discovered that, while DNA lays out the options, many of those life experiences — the foods you eat, the stresses you endure, the toxins you're exposed to — physically affect the DNA and tell it more precisely what to do.

The cause: a kind of secondary code carried along with the DNA. Called the "epigenome," this code is a set of chemical marks, attached to genes, that act like DNA referees. They turn off some genes and let others do their thing. And although the epigenome is pretty stable, it can change — meaning lifestyle choices such as diet and drug use could have lasting effects on how the body works.

"The thing I love about epigenetics is that you have the potential to alter your destiny," says Randy Jirtle, who studies epigenetics at Duke University Medical Center in Durham, N.C.

Twins provide an example of how environment can affect the actions of our DNA. Identical twins have identical genes, but sometimes one twin has autism or cancer while the other remains healthy. Studies show that as twins age, their epigenomes become less and less alike, probably causing a lot of those differences in fate.

Another provocative study: In 2009, researchers at Duke University Medical Center published a study in the journal BMC Medicine on epigenetics and autism. They found that some children with autism had extra DNA referees turning off a gene needed to respond to oxytocin, a hormone important in social interaction. The study was small, including only 40 children, but it suggests that turning off that one gene could cause the social problems people with autism have.

Many pharmaceutical companies are exploring the potential of epigenome-altering medicines: There are already a few cancer drugs that turn off cancer-promoting genes or turn on cancer-fighting ones. But since altering the epigenome could have far-reaching, unintended consequences, many scientists are wary of drugs targeted at less life-threatening conditions.

In short, the study of epigenetics is "booming," says Dana Dolinoy, a toxicologist at the University of Michigan School of Public Health in Ann Arbor.

Pick and choose

The regular DNA genome carries the code for every recipe involved in making a human (or antelope, or philodendron or whatever) — it's like "The Joy of Cooking." But just as some chefs never crack, say, the veggies chapter, while they dog-ear every page on desserts, different parts of the body pick and choose the genes they need.

The epigenome is part of what tells different cells in the body which DNA recipes to read and which to ignore. The small chemicals that attach to the DNA may cover up or restrict access to genes that aren't needed and keep others wide open and readable.

Jirtle compares the system to a computer: The DNA is the hardware — set and unchanging — and the epigenome is the software that tells it when, where and how to work.

Epigenetics might be especially important for pregnant women and infants, because much of the epigenetic code is laid down early in development. Dolinoy speculates that the time before puberty might also be important, since the genome and epigenome are gearing up to launch new genetic programs.

The chemicals that make up epigenetic codes ultimately come from diet. Folic acid, for example, is needed to produce epigenetic molecules that turn off many unwanted genes. Broccoli and garlic are good sources of other types of chemical tags that are part of the epigenome.

In a classic experiment published in 2003 in the journal Molecular and Cellular Biology, Jirtle showed how diet can affect these DNA referees. He studied certain mice that can have either brown or yellow pups. He showed that when pregnant mice eat lots of folic acid and other vitamins, they have mostly lean, brown pups. If those mothers instead eat a diet without the epigenome-enhancing supplements, they have more fat, yellow pups, which are prone to diabetes.

The DNA of the pups is the same — but mom's diet determined how they used those genes.

Dolinoy used the same types of mice to examine how bisphenol A, a toxin common in hard plastics, affects the epigenome of unborn mice. In a 2007 paper in the Proceedings of the National Academy of Sciences, she reported that mice whose diet included bisphenol A produced more fat, yellow pups. But eating folic acid counteracted those negative effects.

Human mothers, not just rodent ones, affect their children's epigenomes. In a study published last year in the American Journal of Respiratory and Critical Care Medicine, scientists at USC's Keck School of Medicine found that if the mother smoked during pregnancy, there were long-lasting changes in her children's epigenomes. The authors speculated that these changes could affect how the body turns on genes for cancer and development.

Dolinoy, who is expecting her second child in May, cautions that women concerned about epigenome changes in their kids should not base health decisions on this still-immature science. For example, she advises not to overdo it with prenatal supplements. While some folic acid is certainly good — it prevents birth defects — too much might alter the epigenome in unknown, undesirable ways.

"My philosophy is, everything in moderation," she says.

A stress factor?

The epigenome can also be altered after a person is born. For example, researchers from McGill University and the Douglas Mental Health University Institute in Montreal found that child abuse can affect DNA referees. In a 2009 paper in the journal Nature Neuroscience, the authors report that 12 people who were abused as children, and later committed suicide, had different DNA referees on a gene needed to cope with stress, compared with 24 people who were not abused. The research implies, although in no way proves, that diminished ability to cope with stress might have been a factor in the suicides.

Adult epigenomes are still somewhat malleable, but they are stable compared with those of developing fetuses and infants. So there's no need to worry that every little action will alter it.

But there are also short-term referees that jump on or off the DNA at a moment's notice. Many scientists consider these refs to be outside the classical definition of "epigenetics," but those chemical changes do affect genes in similar ways. They may change in response to what you had for breakfast today, or the stress you feel after a tough day.

Genes are not just "on" or "off." They can be on just a little bit, on a lot and everything in between. So referees, both the short-term and long-term types, tune genes up or down, rather like the dimmer switch for a lamp.

And many genes can be turned up or down by changes in behavior and environment. For example, researchers at the Preventive Medicine Research Institute in Sausalito, Calif., studied 30 men with prostate cancer. These men declined traditional medical treatment and instead underwent a three-month program that included a healthy diet, moderate exercise and daily stress management.

When the researchers examined gene activity in the men's prostate biopsy samples, they found that 48 genes were turned up and 453 were turned down, compared with gene activity at the beginning of the study. The authors noted that the study, published in the Proceedings of the National Academy of Sciences in 2008, was small and needs to be repeated to be sure of the effects. They also suggested that similar changes might happen in healthy people too, when they alter their behavior.

Though the science of epigenetics is young, scientists think there's good reason to think about how lifestyle choices may affect the epigenome.

It's known already that some referees can be inherited from human parent to child. Praeder-Willi syndrome, for example, is caused when some of Dad's DNA referees or genes are missing. Among other symptoms, people with the syndrome have an overactive appetite that can easily lead to obesity.

And though it hasn't been proved, some scientists suspect that DNA referees laid down generations ago — in your grandparents, for example — are still active in your body today. That is, the epigenome may "remember" the environment Grandpa grew up in and set your genes to match it, even if you have different foods and activities than he did.

Such control over one's DNA is a double-edged sword, Jirtle says. Healthy choices, such as eating right, could lead to helpful referees, but unhealthy activities, such as smoking, could have a negative effect on you — and your descendants.

"You now have a major responsibility … to optimize your epigenome," he says.

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