

SYNOPSIS - EPISODE 5

DNA IS NOT DESTINY: How the Outside Gets Under the Skin



We know that our fetal and early environments are important. But how do they get under the skin? How might a toxic *social* environment actually become part of us?

DNA Is Not Destiny introduces viewers to the exciting new science of epigenetics which is revolutionizing our understanding of human behavior and health and the critical role played by early environments.

The epigenome is a set of chemical compounds that attach themselves to DNA. They play a critical role in gene expression, akin to dimmer switches or volume controls, turning the genes in our more than 200 specialized cell types on or off, instructing genes to shout loudly or whisper.

It turns out that our experiences, particularly during critical periods such as gestation, the early years and puberty can alter not our genes (they're fixed) but the settings of these epigenetic volume controls, often with enduring consequences for future socio-emotional and even physical health.

Early evidence emerged from a set of experiments first performed in Randy Jirtle's lab at Duke University. Dana Dolinoy, now at the University of Michigan, shows us two sets of genetically identical mice pups—except they are not identical. One group has brown fur and is skinny. The other has yellow fur and is obese. Same DNA, different physical types.

Dolinoy describes how they fed the mothers different diets. One diet contained a molecule called a methyl group. They discovered that the methyl group (consisting of one carbon atom and three hydrogens) attached itself to a segment of a gene involved in obesity and yellow fur (named the Agouti gene), shutting it down. The result? Thin mice pups with brown fur.

Then Dolinoy fed the mothers BPA, a chemical found in many plastics. The Agouti gene remained activated and the pups grew up obese and yellow. She added a methyl group to the diet and again modified the epigenome which in turn silenced the Agouti gene. The pups grew up skinny and brown, reversing the effect of the BPA.

Marie Lynn Miranda, provost of Rice University, who researches environmental hazards, points out that pregnant mothers and young children living in neglected, poor neighborhoods are much more likely to be exposed to a host of environmental toxins—lead, mold, vermin, pollution—that risk altering their epigenome with persistent consequences for behaviors and health.

McGill University's Michael Meaney wondered whether *social* environments might also get under the skin and alter gene expression. Could exposure to stressful conditions early in life have enduring effects? Meaney's pioneering experiments involved rats. Meaney and his colleagues studied two groups of rat pups: one group was licked and groomed a lot by their mothers during their first week of life, the others not so much.

Meaney found the low-licked rats grew up to be more skittish, fearful, hypersensitive to noise and reactive to threats, even when there were none. They were more likely to become obese. Darlene Frances, a neuroscientist now at University of California-Berkeley who had worked with Meaney, examines the brains of the rat offspring under a microscope. Despite being genetically identical, the rats' brains differ. We can see in the brains of low-licked rats fewer numbers of a key receptor which absorbs stress hormones (called glucocorticoids) and tamps down the stress response when a threat has passed. With fewer stress hormone receptors, the low-licked rats' tend to stay on a constant fight-or-flight stress hair-trigger.

Frances then performs another experiment for us, similar to one first conducted by David Sweatt at , to see whether resource scarcity might affect the licking and grooming done by rat mothers.

Frances placed her rats in environments lacking the soft materials they need to construct a nest. The mothers became anxious and began a desperate, never-ending search for suitable nest-building materials. The stressed-out mothers didn't lick and groom their young pups as much. Their pups, licked and groomed less, again grew into hyper-vigilant, skittish adolescents with difficulty learning.

The strain of an adverse environment impeded the rat mother's licking and grooming. Her offspring then had trouble turning their stress response off as adolescents. And this triggered a cascade of health and behavioral effects.

But lab animals are one thing, people another.

Marilyn Essex at the University of Wisconsin-Madison led a 20-year study following the children of 500 mostly white, mostly middle-class parents. She and her colleagues found that stressors on parents around the time they gave birth—job insecurity, long work-weeks, role-overload—correlated with elevated cortisol levels and associated emotional and cognitive issues in their children's later lives

– more anxiety, substance abuse, teen pregnancy, learning problems, failure to complete high school.

When Michael Kobor of the University of British Columbia led a team profiling 50 of those adolescents’ epigenomes, he found epigenetic modifications which correlated closely with the adversity and stress reported by the mother when the children were infants, 15 or 16 years before.

This was a first: evidence that the struggles of working parents stress could modify the epigenome of their young children with enduring effects. The “second-hand” stress the children experienced increased their risk for long-term behavioral problems.

Researchers have found a wealth-health gradient in most every country in the world. At each step up the class pyramid the more affluent tend to have better outcomes than the group just below them.

While the evidence is not yet conclusive, it appears that one vector by which inequality gets under the skin is through changes in the child’s epigenome. Darlene Francis observes, “The poorest kids in society are most vulnerable to just about every health outcome we can measure.”

The good news is that epigenetic effects appear reversible. When Dolinoy fed her yellow, obese mice exposed to BPA a healthy diet, they gave birth to thin pups with brown fur. And when Michael Meaney placed his low-licked rat pups in an enriched environment (analogous, he says, to high-quality childcare) those rats did much better as adults.

Most importantly, the epigenome can be modified by its environment. And environments, unlike genes, are not fixed but changeable. They are produced by the economic and political decisions we make as organizations, communities, states and the nation.

Michael Meaney says, “We know for example, that when populations move into more favorable circumstances, when populations are freed somewhat from oppression, politically and socially, they become healthier.”

A growing number of scientists are advocating for improved conditions for young children and their families, for racial and economic justice, so all children have the opportunities they deserve to reach their full potential. Provost Marie Lynne Miranda sums up: “The science is clear. What we need is public policy to follow the science and give us more protective environments for our children.”

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