

EPIGENETICS

AND THE UNDERPINNINGS OF VULNERABILITY

The study of epigenetics, or changes to gene expression that can be influenced by the environment, has turned the nature vs. nurture debate on its head. Now there's yet another twist to the tale, according to new research coming out of the laboratory of Dr. Michael Kobor, PhD, from the Child and Family Research Institute and the University of British Columbia, and conducted in close collaboration with Dr. Joanna Holbrook of the Singapore Institute for Clinical Sciences and Dr. Michael Meaney of McGill University. It turns out that some people's genomes are more susceptible to epigenetic changes than others. This is the kind of finding that can help explain why only some but not all long-term smokers develop lung cancer or why some children fare better than others in the face of early life deprivation or abuse.



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Using samples taken from umbilical cords, the investigators conducted genetic and epigenetic testing on 237 newborns from the Growing Up in Singapore Towards Healthy Outcomes (GUSTO) birth cohort study. They identified 1,423 regions in the genome where the level of an epigenetic modification (known as DNA methylation) was highly variable across individuals. They calculated that approximately 25% of this variability was due to genetic make-up while 75% was due to the interaction between genetic sequence and the environment *in utero*. These environmental influencers included the mother's smoking habits, depression and body mass index (BMI) as well as the baby's birth weight, gestational age and birth order.

VARIATIONS IN VULNERABILITY

"The broad idea," says Marco Battaglia, MD, a psychiatrist who specializes in developmental psychobiology at Laval University in

Quebec City, "is that we have a kind of blueprint in our DNA, and there is some variation in it. On top of that, epigenetics can vary the expression of the gene. But more complicated is the fact that you have a genetic influence on the propensity to be liable to epigenetic programming".

The complex relationship between genes, epigenetics and environment helps explain why certain difficult early life experiences have been shown to be detrimental in some cases but not others. For instance, initially no link between epigenetic changes and maternal depression could be found. But an analysis of subgroups revealed that only people with specific genetic sequences are vulnerable to epigenetic changes from maternal depression. In other words, we are all born with genomes that make us more or less susceptible to environmental stressors, such as maternal depression, that may produce epigenetic changes.

IDENTIFYING VULNERABLE POPULATIONS

"We will perhaps better understand vulnerability and resilience in certain environments when we put together the genetics, epigenetics, and the environment," says Dr. Kobor. "This will allow us to stratify the population and focus on children who are really vulnerable."

This study lays the foundation for measuring genes and epigenetics that are relevant to identifying vulnerable individuals, says Dr. Battaglia. The remaining challenge is to develop operational definitions of environmental factors to allow for the identification, quantification and differentiation of multiple, often interlinked, environmental factors that are likely to be most detrimental in particular populations and which factors should be targeted most heavily in prevention and intervention programs. 🦋

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Ref.: Teh AL, Pan H, Chen L, Ong ML, Dogra S, Wong J, MacIsaac JL, Mah SM, McEwen LM, Saw SM, Godfrey KM, Chong YS, Kwek K, Kwoh CK, Soh SE, Chong MFF, Barton S, Karnani N, Cheong CY, Buschdorf JP, Stunkel W, Kobor MS, Meaney MJ, Gluckman PD, Holbrook JD. The effect of genotype and in utero environment on interindividual variation in neonate DNA methylomes. *Genome Research* 2014;24(7):1064-1074. doi:10.1101/gr.171439.113.