Epigenetics and Childhood Obesity

To the Editor: In his article in the January 2015 issue of *Mayo Clinic Proceedings*, Archer[1] has, in a novel yet age-old construct, succinctly hypothesized the putative role of epigenetics in a complex multifactorial condition, childhood obesity. His hypothesis is in harmony with the results of a recently published systematic overview of the most recent research findings in the area of epigenetics and obesity, which revealed that the propensity toward adult obesity has early developmental origins and follows an intergenerational cycle.[2]

Epigenetics, an increasingly recognized discipline, is defined as heritable regulation of gene expression without a change in the base sequence of DNA.[3] Epigenetic marks can alter the transcription of a particular gene, thereby determining whether the gene is "turned on or off" at a given point in time. Epigenetic mechanisms that are best studied so far include addition or deletion of methyl groups to DNA (this occurs predominantly at CpG sites), posttranslational modifications to histone proteins, and noncoding RNA. Although the DNA sequence of genes in an individual (the genome) is largely stable, the epigenome is dynamic and has the potential to be reversibly modified by exposure to a range of environmental factors.

Over the past decade, increasing effort has been made to understand the role of epigenetic modifications in other complex conditions like cancer, autoimmune rheumatic diseases, and obesity. To date, DNA methylation, either at global, site-specific, or genome-wide levels at single nucleotide resolution, is by far the most studied epigenetic mark in obesity with the help of high-throughput screening methods. Archer's proposed maternal resource hypothesis is a very useful addition to the insight about developmental origins of health and disease via epigenetic modifications programmed by the perinatal environment.

Epidemiological studies, including Project Ice Storm[4] (a study of the effects of prenatal maternal stress exposure to a storm that impacted Quebec in 1998), have already documented the lasting impact of the prenatal conditions via methylation patterns of offspring.[5] Recently, no connection was found between the *FTO* gene and obesity in the Framingham cohort born before 1942 and very strong correlation in those born after 1972, findings that take Lamarck's notion of environment shaping phenotype to an interesting level.[6,7]

The first steps are already being made in identifying potential epigenetic biomarkers for obesity that could be detected at birth. Eventually, this finding may help in predicting an individual's obesity risk at a young age, before the phenotype develops (the "tipping point." as coined by Archer[1]), and opens possibilities for introducing targeted strategies to prevent the condition. It is also now clear that several epigenetic markers are modifiable by changing maternal habits during pregnancy, to turn the unfavorable epigenomic switch off and pass it in an off mode to several subsequent generations.

As Einstein said, "a problem cannot be solved on the same level at which it arose."[8] With Archer's commendable article, we are going beyond Darwinism back by a few centuries to Lamarck's soft inheritance theory, or even all the way to the Vedas, the oldest books in the library of mankind that say, "You are the architects of your destiny" and of the generations to come. Once we unravel all we can about epigenetics as well as we have done with genetics, we may realize we are no closer to understanding the mysteries of our existence and human behavior. What is clear from the burgeoning field of epigenetics is that the historical argument of nature vs nurture might best be reconciled by a context of nature via nurture.

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In reply—Epigenetics and Childhood Obesity

I sincerely welcome the letter from Drs Kaushik, Pettus, and Malkani and the opportunity to continue the increasingly vigorous scientific discourse that my theory[1] has fomented in disciplines as disparate as pediatrics, sociology, evolutionary genetics, and public