

## **Epigenomics: at the crossroad of genomics and nutrition**

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Recent advances in 'omics and bioinformatics are gradually being incorporated into nutritional studies to help us better understand the mechanisms connecting intrinsic (i.e., genetics) and extrinsic (i.e., diet, environment) factors with an individual's health. Some of the advances that perhaps hold more promise to the consolidation of nutritional genomics are those related to epigenetics/epigenomics. There are three main categories of epigenetic marks: DNA methylation, histone modification and non-coding RNA. These epigenetic marks are reversible, and may allow a rapid adaptation to the environment. However, although differential methylation has been associated with several disease phenotypes, and some studies have reported dietary modification in DNA-methylation, how these processes are regulated by diet remains unclear. In addition, there are SNPs at CpG sites that have effects on methylation levels, hence linking genetic variation to epigenetic changes and increasing the number of regulatory factors that need to be considered. As per the non-coding RNAs, miRNAs are currently the most investigated. They have emerged as crucial epigenetic regulators of many process related to disease. Numerous SNPs in miRNA target sites have also been demonstrated to have allele-specific effects. Thus, the minor allele of the SNP rs13702 in the lipoprotein lipase (LPL) 3'-UTR gene disrupts a miRNA recognition element seed site for the human miRNA-410, resulting in a gain-of-function and lower plasma triglycerides. In addition, we reported that PUFA intake interacted with miRNA-410 target SNPs in determining plasma triglycerides, hence supporting an important role of diet on miRNA regulating effects. Moreover, there is evidence of an interrelationship between miRNA expression, DNA methylation, and histone modifications, contributing to a change of paradigm with regard to the mechanisms by which dietary components may influence disease risk. Interestingly, there is some evidence, though controversial, that exogenous miRNA contained in foods may be detected in humans and may have some physiological effects. According to this thinking, diet may also have additional effects in gene-diet interactions due to the action of these exogenous miRNA.

In summary, our current knowledge provides a limited perspective on the mechanisms through which the diet might exert its health/disease-promoting effects. This is due to several factors: firstly, the complex nature of the foods that we consume; secondly, most studies have still not incorporated the more comprehensive and deep approach provided by 'omic technologies. The introduction of these new 'omics is crucial to explain how the diet dynamically modulates gene expression via epigenetic in fine-tuning gene expression and maintaining our phenotypic flexibility.