Dietary regulation of the epigenome for optimal health and disease prevention.

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Perspective

Our diet is a central etiological element for certain cancers, cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) [1]. Scientist are continually elucidating the molecular mechanisms that link nutrition to physiology and pathophysiology, in which the last two decades have given rise to our increased understanding for diet-gene interactions, also termed nutrigenetics or nutrigenomics [2]. Recent advancements in 'omics' technologies have allowed for acquisition of new knowledge aimed at better understanding diet-gene interactions for optimal health and disease prevention. This has given rise to nutri-epigenetics, in which researchers are examining a role for macro (i.e., protein, fats and carbohydrates) and micro (i.e., vitamins, minerals and other food-derived compounds) nutrients in the regulation of chromatin accessibility and non-coding RNAs, which impact gene expression independent of changes to nucleotide sequence [3].

It is well-known that nutrients derived from plant-based foods (i.e., fruits, vegetables and whole grains) benefit health and wellness through regulation of gene expression [4]. However, recent findings have shown that food bioactives derived from fruits and vegetables regulate gene expression via modifications of nucleosomal DNA or histone proteins [2,5,6]. Modifications of DNA or histone proteins by methylation and acetylation can have profound effects on gene expression, without underlying changes to nucleotide sequence, and is termed epigenetics. Food bioactives such as sulforaphane, resveratrol and epigallocatechin gallate (EGCG), found in cruciferous vegetables, grapes and teas, respectively, have all been shown to regulate DNA/histone methylation and acetylation in the control of gene expression in in vitro and in vivo models of cancer and CVD [5,7-10]. More recently, screening approaches were used to successfully demonstrate that many food bioactives can regulate lysine acetylation, in part, through inhibition of histone deacetylase (HDAC) enzymes [8]; the impact of many of these screened food bioactives as epigenetic regulators of disease remains poorly understood.

Similar to plant-based foods, animal-based foods have also been shown to regulate gene expression [11]. One of the most commonly consumed beverages, milk, is one of the first postnatal nutritional foods for all mammals including humans [12]. As such, milk consumption can have a profound impact on human development as well as health and disease [12]. Much of the nutri-epigenetic work regarding milk consumption has focused on the impact of exosome-derived mircoRNAs (miRNAs) in the regulation of maternal nutrition [13]. However, recent reports have suggested that absorption of bovine milk miRNAs increased in human circulation [14]. Baier et al. [14] demonstrated a dose-dependent increase in circulating miR-29b and miR200c in subjects that consumed 0.25, 0.5 or 1 L of milk. This is interesting, as loss of miR-29b and miR200c has been shown to promote cardiac fibrosis and lung and breast cancer, respectively [15-17]. It should be noted that the source of miRNAs, direct RNA transfer vs. a nutrient response, remains controversial and thus further examination is required [18]. Regardless of source (i.e., bovine-derived or endogenous), however, miRNA expression is altered by milk consumption [14,18] and thus these data suggest that bovine milk consumption can impart health benefits to reduce cardiovascular disease and protect against lung and breast cancer through nutri-epigenetic interactions.

There is no doubt that diet impacts human health. Thus, emerging knowledge concerning how nutrition drives epigenetic adaptations to impact inheritance, human development, health and disease has the potential to transform nutrition and dietetic practice.

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