Gene-nutrient interactions and DNA methylation.

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BACKGROUND: Many micronutrients and vitamins are critical for DNA synthesis/repair and maintenance of DNA methylation patterns. Folate has been most extensively investigated in this regard because of its unique function as methyl donor for nucleotide synthesis and biological methylation.

FINDINGS: Cell culture and animal and human studies showed that deficiency of folate induces disruption of DNA as well as alterations in DNA methylation status. Animal models of methyl deficiency demonstrated an even stronger cause-and-effect relationship than did studies using a folate-deficient diet alone. Such observations imply that the adverse effects of inadequate folate status on DNA metabolism are mostly due to the impairment of methyl supply. Recently, an interaction was observed between folate status and a common mutation in the gene encoding for methylenetetrahydrofolate reductase, an essential enzyme in one-carbon metabolism, in determining genomic DNA methylation. This finding suggests that the interaction between a nutritional status with a genetic polymorphism can modulate gene expression through DNA methylation, especially when such polymorphism limits the methyl supply. DNA methylation, both genome-wide and gene-specific, is of particular interest for the study of cancer, aging and other conditions related to cell-cycle regulation and tissue-specific differentiation, because it affects gene expression without permanent alterations in DNA sequence such as mutations or allele deletions.

CONCLUSION: Understanding the patterns of DNA methylation through the interaction with nutrients is fundamental, not only to provide pathophysiological explanations for the development of certain diseases, but also to improve the knowledge of possible prevention strategies by modifying a nutritional status in at-risk populations.

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