

Dietary metabolites derived from gut microbiota: critical modulators of epigenetic changes in mammals

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The mammalian gastrointestinal tract harbors trillions of commensal microorganisms, collectively known as the microbiota. The microbiota is a critical source of environmental stimuli and, thus, has a tremendous impact on the health of the host. The microbes within the microbiota regulate homeostasis within the gut, and any alteration in their composition can lead to disorders that include inflammatory bowel disease, allergy, autoimmune disease, diabetes, mental disorders, and cancer. Hence, restoration of the gut flora following changes or imbalance is imperative for the host. The low-molecular-weight compounds and nutrients such as short-chain fatty acids, polyamines, polyphenols, and vitamins produced by microbial metabolism of nondigestible food components in the gut actively participate in various epigenomic mechanisms that reprogram the genome by altering the transcriptional machinery of a cell in response to environmental stimuli. These epigenetic modifications are caused by a set of highly dynamic enzymes, notably histone acetylases, deacetylases, DNA methylases, and demethylases, that are influenced by microbial metabolites and other environmental cues. Recent studies have shown that host expression of histone acetylases and histone deacetylases is important for regulating communication between the intestinal microbiota and the host cells. Histone acetylases and deacetylases influence the molecular expression of genes that affect not only physiological functions but also behavioral shifts that occur via neuroepigenetic modifications of genes. The underlying molecular mechanisms, however, have yet to be fully elucidated and thus provide a new area of research. The present review provides insights into the current understanding of the microbiota and its association with mammalian epigenomics as well as the interaction of pathogens and probiotics with host epigenetic machinery.

INTRODUCTION

The human gut microbiome is a multifaceted ecosystem that harbors a stunning number of microbes – approximately 100 trillion – representing about 5000 species.¹ An estimated 90% of cells present in the human body are of prokaryotic origin, belonging to some 40 000 bacterial strains in 1800 genera.^{2,3} The collective number of these microbes is far greater than the total number of

host cells, and both the number and the diversity of these microbes play an important role in the establishment and maintenance of body health. Gut microorganisms co-evolve with their host and are imperative for the development of a healthy gut. They are also important for normal daily gastrointestinal tract functions such as digestion, absorption, and immune function as well as for protection against colonization by pathogens.⁴ These microbes also synthesize important

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