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Donohoe and colleagues used a gnotobiotic mouse model colonized with bacteria that converts fiber into butyrate to show that a high-fiber diet does protect against colorectal tumorigenesis but that the effect is dependent on butyrate and the composition of the gut microbiota. Butyrate serves as the main mitochondrial energy source for normal colonocytes but accumulates in cancer cells, which are instead dependent on glucose due to increased glycolysis associated with the Warburg effect. Accumulation of butyrate, an endogenous histone deacetylase inhibitor, is associated with increased histone acetylation in colorectal tumors and increased expression of genes with known roles in apoptosis and cell-cycle arrest. These findings indicate that dietary fiber can protect against colorectal cancer and suggest that gut microbiome studies should be integrated with future epidemiologic studies on fiber and colorectal cancer risk. For details, please see the article by Donohoe and colleagues on page 1387.

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