The estimated trillions of microbes that inhabit the human body establish a beneficial relationship with the host, but it is clear that dysbiotic relationships can develop, some of which are thought to result in the development of inflammatory diseases and cancer. Several case-control metagenomics studies suggest that dysbiosis in the commensal microbiota is associated with inflammatory disorders and various cancer types throughout the body. The cover image is an artist’s adaptation of a portion of Figure 1 from the Review in this issue, “The Human Microbiome and Cancer,” by Nelson and colleagues (beginning on page 226) and depicts the injection of effector cells by microbes (e.g., H. pylori) with subsequent modulation of various pathways, including Wnt/β-catenin and autophagy, to promote carcinogenesis. One mechanistic link between the microbiome and cancer is via the immune system, as the resident microbiota plays an essential role in activating, training, and modulating the host immune response. Immunological dysregulation is likely to provide mechanistic explanations as to how our microbiome influences cancer development and cancer therapies. The review discusses the complex connection between the human gut microbiome and cancer as well as the feasibility of developing novel cancer diagnostics based on microbiome profiles.