Spotlight

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Intestinal Inflammation and Cancer

Westbrook *et al.*
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Chronic intestinal inflammation serves as a key mediator of the middle stages of tumor development. It increases the risk of local tumors as well as extraintestinal manifestations such as lymphomas, other solid cancers and autoimmune disorders. However, the mechanistic details are still blurry. So far, the clearest evidence of a link between cancer and inflammation is the data demonstrating that such inflammation increases genotoxic stress, as previously shown by the authors of the current study and others.

Digging deeper, Westbrook *et al.* analyzed subpopulations of leukocytes in peripheral blood as well as cells from various distant lymphoid and nonlymphoid tissues for single- and double-stranded DNA breaks in several experimental models of intestinal inflammation. Cells most sensitive to the mutagenic impact of chronic intestinal inflammation were $CD8^+$ peripheral leukocyte subpopulations but they also found DNA damage in other cells of lymphoid organs, intestinal epithelial cells and hepatocytes. Further experiments suggested that the observed genotoxicity was induced by increased levels of systemically circulating proinflammatory cytokines and was due to increased DNA damage rather than to decreased DNA repair.

Although further studies are required to define the exact molecular mechanisms that turn inflammation from a powerful defense mechanism that helps eliminate pathogens into a co-conspirator in the process of carcinogenesis, the findings add another piece to the puzzle of how chronic intestinal inflammation increases genotoxic stress in remote tissues.