LUCY READING-IKKANDA

WHERE CANCER AND INFLAMMATION INTERSECT

Recent clinical trials have reignited the interest in simple anti-inflammatory drugs like aspirin for controlling the inflammation associated with cancer. The results suggest that these drugs reduced the risk of relapse as well as cancer formation across many types of cancer. However, aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) can have severe gastrointestinal and cardiovascular side effects, so researchers have been looking for other ways that cancer and inflammation intersect in the hope of finding a better target for therapy.

FROM CHRONIC INFLAMMATION TO CANCER

Inflammation, which can be initiated by innate-immune receptors such as the Toll-like receptors (TLRs), results in the activation of a wide range of aggressive immune cells (via IL-6 and other cytokines). Inflammation also induces changes in blood vasculature (including the growth of new vessels via VEGF) that allow immune cells to exit the blood stream and penetrate tissue (via E-selectin and VCAM-1). Those inflammatory signals that promote cell division and repair also create an environment that promotes cancer formation and growth (via ROS and metalloproteases). The major gene that drives the inflammatory pathway codes for the transcription factor NF-κB, which activates a number of inflammatory genes, including the genes for the COX enzymes that boost inflammation and are inhibited by aspirin. When expressed by cancer cells, STAT3 reacts to inflammatory cytokines like IL-6 by initiating a number of pathways that favor cell replication in the face of mutations that would normally halt growth or initiate cell suicide via apoptosis.