CANCER PREVENTION RESEARCH

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ABOUT THE COVER

Nonalcoholic steatohepatitis (NASH) is a severe form of fatty liver disease characterized by inflammation, steatosis, and fibrosis and balloon degeneration from hepatocyte injury. NASH increases the risk for development of cirrhosis and hepatocellular carcinoma (HCC). Currently, there are no FDA-approved agents to reverse hepatic fibrosis and NASH. In this issue, an investigation by Gay and colleagues (starting on page 17) demonstrates a novel approach to preventing HCC by treatment with a cholecystokinin receptor antagonist, proglumide. Treatment of mice with proglumide reversed NASH; lowered hepatic inflammatory cytokines and chemokines; reduced oxidative stress; and prevented HCC. The anti-fibrotic, anti-inflammatory, and anti-proliferative effects of proglumide may provide hope for future studies to reverse hepatic fibrosis and prevent HCC. Proglumide has a broad safety profile in human subjects and could therefore easily be repurposed for prevention of HCC. The cover histological images show peri-portal fibrosis altering the microenvironment in the liver of a mouse with NASH (left panel) and prevention of these histologic changes with proglumide therapy (right panel).