

Colon carcinogenesis: Influence of Western diet-induced obesity and targeting stem cells using dietary bioactive compounds.

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Abstract

Colon cancer strikes more than 1 million people annually and is responsible for more than 500,000 cancer deaths worldwide. Recent evidence suggests that the majority of malignancies, including colon cancer are driven by cancer stem cells (CSCs) that are resistant to current chemotherapeutic approaches leading to cancer relapse. Wnt signaling plays a critical role in colon stem cell renewal and carcinogenesis. Leucine-rich repeat-containing G protein-coupled receptor 5 (LGR5), a Wnt target gene, and aldehyde dehydrogenase 1 B1 (ALDH1B1) are good markers for normal and malignant human colon stem cells. Diet contributes to 20% to 42% of all human cancers and 50% to 90% of colon cancer. Recent evidence shows that the Western diet has a causative link to colon cancer; however, mechanisms of action are not fully elucidated. Western diet-induced obesity elevates systemic insulin-like growth factor-1 and insulin levels, which could lead to elevated proliferation and suppressed apoptosis of CSCs through PI3K/AKT/Wnt pathway. Although conventional chemotherapy targets the PI3K/AKT pathways and can significantly reduce tumor size, it fails to eliminate CSCs and has serious side effects. Dietary bioactive compounds such as grape seed extract, curcumin, lycopene, and resveratrol have promising chemopreventive effects, without serious side effects on various types of cancers due to their direct and indirect actions on CSC self-renewal pathways such as the Wnt pathway. Understanding the role of CSCs in diet-induced colon cancer will aid in development of evidence-based dietary chemopreventive strategies and/or therapeutic agents targeting CSCs. Copyright © 2014 Elsevier Inc. All rights reserved.

KEYWORDS:

Colon cancer; Curcumin; Grape seed extract; IGF-1; Insulin; LGR5, ALDH1B1; Lycopene; Resveratrol; Stem cells; Western diet; Wnt