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Targeting the crosstalk between canonical Wnt/β-catenin and inflammatory signaling cascades: A novel strategy for cancer prevention and therapy

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ABSTRACT

Emerging scientific evidence indicates that inflammation is a critical component of tumor promotion and progression. Most cancers originate from sites of chronic irritation, infections and inflammation, underscoring that the tumor microenvironment is largely orchestrated by inflammatory cells and pro-inflammatory molecules. These inflammatory components are intimately involved in neoplastic processes which foster proliferation, survival, invasion, and migration, making inflammation the primary target for cancer prevention and treatment. The influence of inflammation and the immune system on the progression and development of cancer has recently gained immense interest. The Wnt/β-catenin signaling pathway, an evolutionarily conserved signaling strategy, has a critical role in regulating tissue development. It has been implicated as a major player in cancer development and progression with its regulatory role on inflammatory cascades. Many naturally-occurring and small synthetic molecules endowed with inherent anti-inflammatory properties inhibit this aberrant signaling pathway, making them a promising class of compounds in the fight against inflammatory cancers. This article analyzes available scientific evidence and suggests a crosslink between Wnt/β-catenin signaling and inflammatory pathways in inflammatory cancers, especially breast, gastrointestinal, endometrial, and ovarian cancer. We also highlight emerging experimental findings that numerous anti-inflammatory synthetic and natural compounds target the crosslink between Wnt/β-catenin pathway and inflammatory cascades to achieve cancer prevention and intervention. Current challenges, limitations, and future directions of research are also discussed.