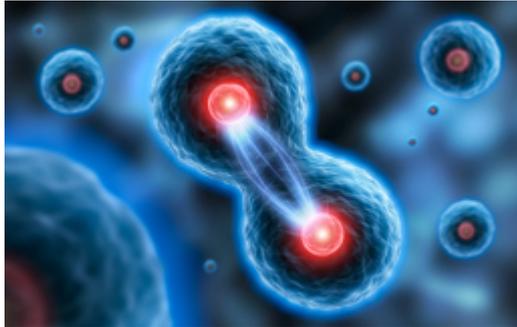




Targeting Oncogenic Transcriptional Programs Through Tissue Specificity

TECHNOLOGY NUMBER: 2021-208



OVERVIEW

Targeting oncogenic transcriptional programs through tissue specificity

- Identification of a tissue-specific axis of the Wnt/beta-catenin signaling complex
- Provides a process to increase the therapeutic index of affected cancer patients

MODALITY

Pharmacological intervention (such as small molecule inhibitors or biologics), applied systemically or locally depending on cancer type and tissue accessibility

INDICATION

Treatment of Wnt-driven cancers, including those resistant to standard chemotherapies

PUBLICATIONS

["β-Catenin-Driven Differentiation Is a Tissue-Specific Epigenetic Vulnerability in Adrenal Cancer"](#)

INTELLECTUAL PROPERTY

Patent pending

BACKGROUND

The wingless-related integration site (Wnt) and its central component beta-catenin form an evolutionarily conserved mechanism that plays an important role in cellular homeostasis. Wnt/Beta-catenin regulates embryo development, cell proliferation and differentiation,

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Therapeutics and Vaccines
Life Sciences

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apoptosis, and inflammation-associated cancer. It is highly activated in about 20% of human neoplasms and promotes proliferation of cancer stem cell subsets in tumors. Wnt signaling is associated with tumor resistance to cytotoxic chemotherapy and to the influences of immune-mediated effects. Wnt signaling has been targeted as a method for anti-cancer therapy, though the resulting changes in non-cancer cell homeostasis have caused toxicity that has limited this approach. Therefore, a need exists to develop successful anti-tumor targets through Wnt signaling using a tissue-specific approach to limit adverse effects.

INNOVATION

Researchers at the University of Michigan have identified a novel, tissue-specific axis of the Wnt/beta-catenin programming that creates signaling in oncogenic tissues while not impacting healthy tissues. Through comprehensive molecular profiling studies, this technology identified targets of Wnt signaling that rely on a physical interaction between beta-catenin tissue-specific transcription factors. In cells, beta catenin is recruited to active enhancers in a tissue-specific, transcription-factor dependent manner. Perturbation of this interaction through any one of multiple pharmacological approaches can cause loss of tissue-specific transcriptional programming, reduced viability, and diminished sustained proliferation potential in vitro. These data suggest that the ultimate consequence of Wnt pathway alterations in Wnt-drive cancers is co-optation and mis-engagement tissue-specific transcription factors to reinforce pro-proliferative oncogenic programming. Therefore, this novel approach described by the inventors provides a strategy that increases the therapeutic index and likelihood of success targeting this pathway in future clinical trials.