

Frizzled receptor modulators: Clinical agents as a basis for development of new Wnt/frizzled function regulators

Value proposition

Wnt signaling is an essential signaling pathway for all multicellular animals. Frizzled receptor is a cell surface receptor that can interact with Wnt to mediate the developmental, morphogenetic, and tissue-regenerative effects of Wnt signaling. Dysregulated Wnt signaling is associated with many cancers. Wnt over activated animal models develops tumor suggesting a causative role for Wnt in tumorigenesis. Moreover, multiple types of cancer including but not limited to colon, cervix, kidney, blood, prostate cancer, have elevated Wnt/Frizzled activity. Further, previous studies have demonstrated Wnt/Frizzled signaling is essential for the survival and progression of multiple types of cancer cells. Therefore, inhibiting Wnt/Frizzled signaling may lead to a potential cancer treatment. As a cell surface protein, Frizzled is an accessible and appealing drug target. However, there are currently no FDA-approved drugs or antibodies that regulate Wnt/Frizzled signaling.

Technology

Chen lab discovered that the FDA-approved compound Niclosamid, a compound previously used to treat tapeworms, and its relative compounds can serve as inducers to internalize Frizzled. In other words, Niclosamid causes Frizzled to be taken into the cell from cell surface, and thus inhibiting its interaction with Wnt. As a result, Niclosamid can be used to inhibit Wnt/Frizzled signaling and potentially inhibit cancer cell growth and survival. Chen lab has demonstrated that Niclosamid can effectively target Wnt/Frizzled signaling in tumor cells. Tumor cell lines and animal models have strongly responded to Niclosamid treatment. In addition, the present invention also includes multiple forms of Niclosamid and thus expanding the compounds that can be used for Wnt/Frizzled related cancer treatment. This invention provides a novel therapy for Wnt/Frizzled related cancer and can be combined with other treatments to kill tumor cells more effectively.

Other applications

The present invention also provides a method of treating other diseases with abnormally elevated Wnt/Frizzled signaling:

- Cardiovascular diseases
- Research tools in the study of the physiological consequences of Wnt signaling

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Advantages

- Niclosamid is a FDA approved drug
- High reliability with detailed pharmacokinetic analysis in cell and animal models
- A variety of Niclosamid related compounds are ready to be used in therapeutic development