Niclosamide conjugated peptides

Duke LICENSING & VENTURES

Value Proposition

Colorectal cancer is the third most commonly diagnosed malignancy and fourth leading cause of death. Abnormal Wnt signaling activity is a major mechanism responsible for many diseases. It is dysregulated in more than 80% of colorectal cancers. Given the importance of Wnt signaling pathway in colorectal cancer, therapies to target this pathway are medically needed. Niclosamide is a drug traditionally used in parasitic infections that has been shown to inhibit Wnt signaling and suppresses colon cancer cell growth. Although the pharmacokinetic properties of niclosamide are appropriate for use as an anthelmintic, its low solubility, low bioavailability and low systemic exposure limit its usefulness in cancer therapy. New formulations of niclosamide for use in systemic diseases have been reported, but these formulations did not result in significant improvement of pharmacological properties.

Technology

Duke researchers have developed a novel formulation niclosamide for the treatment of colorectal cancer. Niclosamide loaded polypeptide nanoparticles were synthesized by conjugating the drug to recombinant chimeric polypeptides. Niclosamide-conjugated polypeptide nanoparticles delivered intravenously dramatically increased the solubility and pharmacokinetic properties of the drug. The new formulation significantly extended the duration of exposure as compared to free NIC after intravenous administration, and enhanced the efficacy of the drug in reducing tumor growth of human colon cancer xenografts in mice.

Other Applications

Improvement of the pharmacological and pharmacokinetic properties of Niclosamide could make more widespread use of this drug in multiple diseases. These may include other types of cancer, bacterial and viral infection, type II diabetes, endometriosis, neuropathic pain, rheumatoid arthritis, sclerodermatous graft-versus-host disease, nonalcoholic fatty liver disease, and systemic sclerosis.

Advantages

- Elastin-like polypeptides as fusions to peptide drugs are well tolerated in humans and do not induce a significant immune response in most individuals

Duke File (IDF)

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Links

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- Niclosamide-conjugated peptides significantly increase the plasma exposure of the drug as compared to free niclosamide
- Exhibit greater anti-cancer activity in colon cancer xenograft model, with no observable adverse effects

Publications

- Niclosamide-induced Wnt signaling inhibition in colorectal cancer is mediated by autophagy (Biochemistry Journal, 2019)
- Niclosamide-conjugated polypeptide nanoparticles inhibit Wnt signaling and colon cancer growth (Nanoscale, 2017)
- The Anti-Helminthic Niclosamide Inhibits Wnt/Frizzled1 Signaling (Biochemistry, 2009)