INNOVATION PARTNERSHIPS
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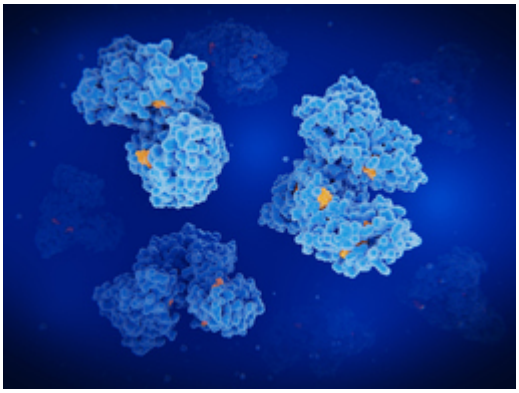
Novel Drug Formulation

TECHNOLOGY NUMBER: 2019-436



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Category
Therapeutics and Vaccines
Life Sciences

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OVERVIEW

A novel albumin nanoformulation of APG-152 which acts as an antineoplastic agent

- Permits aqueous solubility for an agent known to have usefulness against solid tumors
- Exhibits synergy with cytotoxic chemotherapy agents and can be used in combined regimens

BACKGROUND

Programmed cell death, or apoptosis, is controlled by proteins in the B-cell lymphoma-2 (BCL-2) family which undergo direct binding interactions that regulate mitochondrial outer membrane permeabilization (MOMP). These reactions lead to the irreversible release of intermembrane space proteins that cause caspase activation and subsequent apoptosis. Many cancer cells are dependent on the expression of anti-apoptotic BCL-2 family proteins for their growth, so this series of pathways has been a focus of anti-neoplastic interventions.One goal has been to develop small molecule modulators of the BCL-2 family proteins, and a highly potent investigational small molecule named APG-1252 which binds to the BCL gene family has been studied in this setting. APG-1252 has been shown to have a broad therapeutic potential for treatment of solid tumors, though it has been limited in clinical applications due to its poor aqueous solubility. A need exists to improve the ability of this molecule to be distributed at therapeutic level in vivo.

INNOVATION

Researchers report that they have synthesized an albumin nanoformulation of APG-1252 which can reach acceptable levels of solubility to act as a therapeutic agent. The size of the nanoformulation can be tuned between various concentrations by changing manufacturing

process parameters. The inventors have observed and documented the stability of the formulation, including the stability in solution, the dilution stability, and long-term stability in storage. They also conducted a cytotoxicity study in tumor cells to prove the equivalence of antitumor efficacy between the nanoformulation and free drug.The discovery mimics the experience of the albumin nanoformulation of paclitaxel Abraxene, which has been delivered successfully in the clinical setting for several years. Preclinical studies have shown that APG-1252 alone achieves complete and persistent tumor regression in multiple tumor xenograft models in solid tumor types such as small cell lung cancer (SCLC), colon, breast, and acute lymphoblastic leukemia (ALL). The nanoformulation achieves strong synergy with cytotoxic chemotherapeutic agents, suggesting that APG-1252 may have a broad therapeutic potential for the treatment of human cancer as a single agent or in combination with other classes of anticancer drugs.

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