Biomedical

VCU Innovation Gateway
Office of Research and Innovation

Novel Anti-Cancer Stem Cell Agents

The cancer stem-like cell (CSC) hypothesis explains the shortcomings of current anti-cancer therapeutics and posits a paradigm-shifting direction for the discovery of new anti-cancer drugs. The major shortcomings of the current anti-cancer chemotherapy are the primary and acquired resistances to cytotoxic agents, which lead to disease recurrence. This phenomenon is thought to arise from the very small population of CSCs that possesses the ability to self-renew, differentiate and reconstitute the entire tumor after initial treatment. Clearly, a therapeutic that selectively targets CSCs to inhibit their self-renewal and differentiation potential is key to preventing relapse and thereby greatly enhancing survival.

The technology platform

Researchers at Virginia Commonwealth University have designed, synthesized and shown that **distinct and unique novel sulfated flavonoids inhibit CSC self-renewal and differentiation, thereby preventing cancer relapse.** The unique sulfated flavonoids modulate the interaction of glycosaminoglycans (GAGs) with cell surface receptors that are involved in growth and/or differentiation signaling, resulting in the reduction of the incidence of cancer recurrence due to CSCs. The sulfated flavonoids are easy to synthesize, easy to transform into formulations, and easy to monitor *in vivo* for PK/PD. The efficacy of these novel sulfated flavonoids has been demonstrated in several murine models of colorectal cancer. A series of patent applications have been filed to protect the technology platform.

The specific technology

A lipidic quercetin dimer, labeled as **G5C, prevents relapse of cancer in nearly 100% of animals** when xenografts are induced with cells previously treated with anti-cancer agents (5-fluorouracil and oxaliplatin (FUOX)). Likewise, G5C and other specific analogs significantly reduce xenograft growth alone and in combination with FUOX. G5C is a lipidic analog of a sulfated quercetin dimer, which potently and selectively inhibits colorectal, pancreatic, and lung CSCs. G5C exhibits strong anti-CSC activity (~50 – 100 mg/kg) without any significant toxicity (at ~3-times the effective dose); has a half-life of > 6 h; oral bioavailability 20 – 30%, and a shelf-life of > 3 months. G2C and G8C are two other unique analogs of G5C that are currently being studied in multiple models of cancer and therapeutic efficacy.

Benefits

- Target and inhibit cancer stem-like cells without affecting normal stem cells
- Novel glycosaminoglycan mimetics with selective inhibitory effects
- Target fundamental pathways crucial to cancer stem cells survival, renewal and induction of differentiation
- Small molecules and easy to synthesize

Applications

- Supplement ongoing chemotherapy and/or radiation treatment
- Augment treatment of refractory cancers
- Second-line drug to prevent cancer recurrence
- Treatment of a variety of cancers where the cancer stem-like cell paradigm is operative
  - Colon, breast, pancreatic, lung, and brain cancers

Patent status:
Patent issued for novel sulfated flavonoid oligomers: U.S. rights are available. 9850221

Patenting pending for lipidic quercetin dimer: U.S. and foreign rights are available.

License status:
This technology is available for licensing to industry for further development and commercialization.

Category:
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