

CARP-1/CCAR1 Functional Mimetics (CFMs): Novel small molecule suppressors of human breast cancer cell growth.

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Technology description

Background

CARP-1 (Cell cycle and apoptosis regulator protein) is a regulator of cell growth signaling. The researchers have found that CARP-1 inhibits cell growth by binding with the anaphase promoting complex (APC)-2 protein. Since breast cancers often have dysregulated cell cycle signaling, the researchers hypothesize that CARP-1 mimetics that target APC-2/cell cycle signaling will inhibit HBC cell survival pathways. The researchers' work has shown that CARP-1 is a regulator of apoptosis induced when proliferation signaling by epidermal growth factor receptor (EGFR) is inhibited. The EGFR family of proteins is a known risk factor for development of disease, predictors of prognosis and response to therapy, and is utilized as therapeutic targets against a variety of cancers including breast cancer. CARP-1 mimetics are anticipated to facilitate effective targeting of key oncogenes (APC-2) and will serve as efficacious anti-tumor agents for treatment of breast cancer alone or in conjunction with chemotherapy agents such as Adriamycin, Herceptin, Iressa, Lapatinib, and Erbitux. The researchers hypothesize that CARP-1 is a novel suppressor of HBC growth and is a key regulator of Adriamycin as well as EGFR signaling pathways. CARP-1 mimetics have the potential to sensitize chemotherapy-resistant cancers for growth inhibition. Thus, a combination of CFMs and agents like Adriamycin or Herceptin is anticipated to be superior in inhibition/killing of diverse phenotypes of breast cancer, including the drug-resistant cancers. The researchers want to develop novel, cell permeable small molecule mimetics of CARP-1 function for efficient and safe targeting of breast cancers by exploiting cell growth inhibitory targeting of APC-2 proteins by CARP-1.

Technology

The innovation and challenge of the approach was to identify molecules that mimic CARP-1 function and were capable of inhibiting oncogenic signaling by the APC cyclosome pathway. Since an oncogene is required for survival of cancer cells, targeting of the oncogene pathway by CARP-1 mimetics will exploit the Achilles heel of cancer. The APC cyclosome pathway is a crucial regulator of cell cycle progression and various cell cycle check-point controls are often compromised in a range of cancers, including the breast carcinomas. The APC-ubiquitin ligase complex is a hotly pursued target for therapeutic intervention in cancers. A chemical library of over 10,000 compounds was screened and three were selected.

Application area

CARP-1 plays an important role in apoptosis (cell death) induction in human breast cancer (HBC) cells in the presence of the chemotherapy agent Adriamycin.

Advantages

CARP-1 mimetics are a new target intervention strategy with possibilities for affecting multiple cancers. It is a small molecule with demonstrated in vivo activity. It is already synthesized. The molecule can be delivered by IV. It has shown improved efficacy and therapeutic index of current chemotherapeutic agents such as Adriamycin and Velcade. There is a possible application for use combating drug resistance.

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