"Inhibitor of C-terminal Binding Protein (CtBP) as a Novel Potent Anti-Cancer Agent."

VCU #14-005

Applications

- Novel chemotherapy agent for cancers with upregulated CtBP, including colon, breast and ovarian cancers
- Can be used as a primary or adjunctive chemotherapy

Advantages

- Novel enzyme target class
- Multi-target mode of action
- Less cytotoxic to normal cells
- Most potent CtBP inhibitor to date
- Cell membrane permeable
- Established crystal structure of a complex with CtBP, allowing for molecular modeling and targeted compound synthesis

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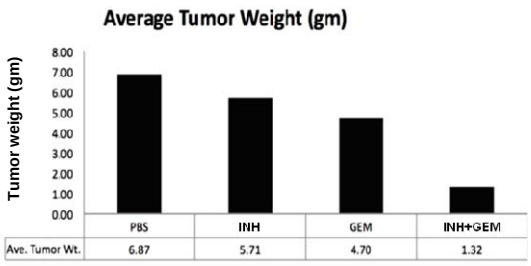
Market Need

Most of the currently available cancer chemotherapies are focused on inhibition of activated oncogenic kinases (e.g. Bcr-Abl, Ras, EGFR). Dehydrogenases are not yet the target of any approved or marketed drugs. C-terminal Binding Protein (CtBP) is one of a few dehydrogenases under development as a molecular target in cancer. CtBP has a transcriptional repressor activity of multiple tumor suppressor genes and a dehydrogenase enzyme core. Thus, inhibition of CtBP with just a single molecule allows for re-activation of multiple anti-cancer genes. Small-molecule therapeutics that restore the function of natural tumor-suppressor genes are becoming promising mono- or combination therapy for cancer.

Technology Summary

Inventors from VCU established a lead molecule in a new drug class of CtBP inhibitors. This molecule is the most potent, cell-permeable CtBP inhibitor ever reported. By blocking transcriptional activity of CtBP, it restores expression and function of tumor suppressive genes, such as *Bik* and *E-cadherin*. In an *in vivo* colon cancer mouse xenograft model, treatment with this inhibitor substantially reduces tumor weight, especially when used in combination with the standard chemotherapy agent, gemcitabine. Reinstating the function of tumor suppressor genes brings back the natural ability of cells to counter oncogenic transformation. Since CtBP overexpression was found in cancerous tissues from several types of cancer (e.g. colon, breast, ovarian, lung, head and neck squamous cell, prostate, and melanoma) but not in adjacent healthy tissues, the CtBP inhibitors are tumor-selective and have fewer off-target effects compared to many current chemotherapeutics. Potent CtBP inhibitors can be utilized as primary or adjunctive therapies in various cancers where CtBP is upregulated, including colon, breast, and ovarian cancers.

Efficacy of novel CtBP inhibitor in mouse xenograft model.



Treatment started one week after mice inoculation with $p53^{-/-}$ HCT116 cells ($3x10^6$). Tumor burden was assessed by measuring total peritoneal tumor weight. PBS, saline; INH, CtBP inhibitor; Gem, gemcitabine.

Technology Status

In vitro and *in vivo* testing has been performed on the proposed molecule in relevant animal models.
Patent pending: U.S. and foreign rights available.
This technology is available for licensing to industry for further development and commercialization.