UNIVERSITY OF MARYLAND
UM VENTURES
MPOWERING THE STATE

www.umventures.org

New Compounds to Treat Metastatic and Triple Negative Breast Cancer

Summary

Despite multi-modal treatment, approximately 40% of all women with breast cancer will suffer a recurrence. While the 10-year overall survival rate for women without recurrence is 84%, this drops to 49%-72% for women with a locoregional recurrence or a second primary malignancy. Luminal breast cancer has the highest rates of relapse, often localizing to the bone, and accounts for 50% of all metastatic-related breast cancer deaths. Strategies that target pathways involved in metastasis and cancer stem cell differentiation, in addition to treating the primary malignancy, may prevent or slow the rate of recurrence. New approaches are especially needed to help patients with triple-negative breast cancer (TNBC), as TNBC's inherently aggressive clinical behavior and the lack of recognized molecular targets for therapy lead to a poorer outcome. To this end, UMB researchers have used computer-aided drug design to identify a lead compound, CADD522, that targets RUNX2, a transcription factor and member of the RUNT family of genes that plays a vital role in breast carcinogenesis and metastasis. RUNX2 is a validated target for breast cancer that is expressed in luminal, triple negative and HER2+ breast cancer. Its expression is associated with poor survival in patients with both luminal breast cancer and TNBC. CADD522, is a potent, high-affinity inhibitor that blocks the ability of the RUNX2 transcription factor to drive breast cancer proliferation and mammosphere formation.

Key Investigator

Antonino Passaniti
Alexander MacKerell

Field

Therapeutics

Technology

Small molecule RUNX2 transcription factor inhibitor

Status

Available for licensing
Available for sponsored research

Patent Status

Pending,
PCT/US2016/023257

UMB Docket Reference

AP-2015-080

External References

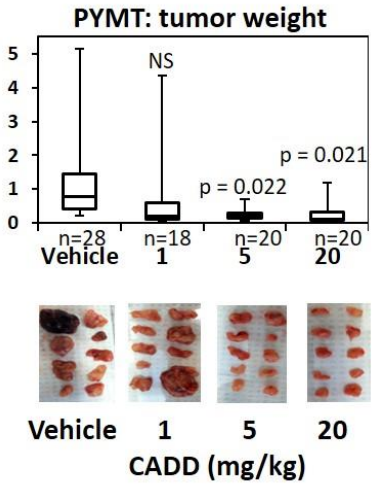
Underwood KF et al. (2013) *JoVE*. 31(78).

Market

Since 1995, 23 drugs have been approved by the FDA for the treatment of breast cancer. Despite this diversity in therapeutic approaches and multi-modal treatment, breast cancer remains the second leading cause of cancer-related deaths among women. Approximately 12.4% of women in the US are expected to be diagnosed with breast cancer at some point during their lifetime. By 2021, the global breast cancer drug market is expected to grow to $17.2 billion, driven by increases in the cost of annual treatment as the use of combinations of branded therapies, for both early-stage and metastatic disease, continues to be favored.

Technology

Using computer-aided drug design, compound CADD522 was identified as a potential anti-cancer compound targeting RUNX2:DNA- binding domain. CADD522 has been extensively characterized *in vitro*, where it exhibits an IC_{50} of 10 nM in RUNX2 DNA binding assays and 5-10 µM potency in breast cancer cell lines (MDA-MB-468, MCF7, and HCC1428). *In vitro* data show CAD522 inhibits the migration of breast cancer cells and the formation of tumorspheres. *In vivo*, CAD522 administration decreases the number of tumors and their weight in the MMTV/ PyMT mouse model of breast cancer (see figure).



Advantages

CADD552 shows both oncolytic and anti-proliferative properties.
RUNX2 is not expressed in normal, differentiated tissues such as breast and prostate.
RUNX2 is expressed in a wide range of cancers including lung, prostate and colorectal cancer.
RUNX2 cooperates with other oncogenic factors; therefore, compounds may be administered in combination with other cancer drugs.

Contact: mblackman@umaryland.edu
410-706-6277

University of Maryland, Baltimore
620 W. Lexington St., 4th Floor
Baltimore, MD 21201