

## NOVEL SMALL MOLECULE ANTAGONISTS TARGETING METASTASIS-ASSOCIATED LUNG ADENOCARCINOMA TRANSCRIPT 1 (MALAT1) LONG NON-CODING RNA (LNCRNA) AS ANTICANCER AGENTS

### SUMMARY (1024-CHARACTER LIMIT)

Researchers at the National Cancer Institute (NCI) have developed an invention describing compounds that bind and alter the nuclear copy number of a long non-coding RNA (lncRNA), metastasis-associated lung adenocarcinoma transcript 1 (MALAT1), with the proposed consequence of inducing slower tumor growth and a reduction in metastasis. The NCI seeks licensing and/or co-development research collaborations for novel small molecule antagonists targeting MALAT1 lncRNA as anticancer agents.

### NIH REFERENCE NUMBER

E-060-2018

### PRODUCT TYPE

- Therapeutics

### KEYWORDS

- Human Metastasis-associated Lung Adenocarcinoma Transcript 1, MALAT1, Long Non-coding RNA, lncRNA, Cancer, Metastasis, RNA, Small Molecule Antagonist, RNA binding small molecule, Specific Binding to MALAT1, Nuclear Retention Element, ENE, Le Grice

### COLLABORATION OPPORTUNITY

This invention is available for licensing and co-development.

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### STATUS

Active

### DESCRIPTION OF TECHNOLOGY

Human metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) is a long non-coding RNA (lncRNA) overexpressed in multiple human cancers. There is a strong correlation between MALAT1 levels and increased risk of various malignancies including metastasis. Antisense oligonucleotide

inhibition of MALAT1 expression levels has shown promising anticancer effects in vivo. Additionally, depletion of MALAT1 is not lethal to normal cell growth, further supporting MALAT1 as a promising therapeutic target for cancer therapy.

The enhancement of oncogenic processes by MALAT1 in cancers has been localized to its 3'-end sequence. The structure of this region is suggested to contribute to RNA stability, and that triple helix formation blocks exonucleolytic RNA degradation. MALAT1 3'-end triple helix formation was confirmed with a recent crystal structure showing the 3'-end A-rich region engaged in a triple helix with nuclear retention element (ENE). Development of small molecules that recognize and disrupt MALAT1 triple helix structure (designated MALAT1 ENE), and ultimately its degradation, would provide novel therapeutics for cancers associated with enhanced levels of MALAT1.

Researchers at the National Cancer Institute (NCI) have developed an invention describing the identification of MALAT1 ENE binding ligands. The ligands have been further studied for their ability for reverse branching morphogenesis in tumor-derived organoids. The inventors have demonstrated a ~50% drop in the nuclear MALAT1 copy number after treatment with MALAT1 ENE binding ligands. Furthermore, the inventors have shown that small molecules targeted to MALAT1 do not recognize a triple helix encoded by a similar lncRNA, NEAT1.

## POTENTIAL COMMERCIAL APPLICATIONS

- Anticancer agent
- Small molecule antagonists targeting MALAT1 lncRNA

## COMPETITIVE ADVANTAGES

- To date, no specific small molecules capable of affecting MALAT1 nuclear copy number have been reported
- Novel small molecules with the potential to disrupt the function of a cellular long noncoding RNA implicated in several cancers
- No small molecules specific to MALAT1 as opposed to structurally-related RNA triple helices have been reported

## INVENTOR(S)

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## DEVELOPMENT STAGE

- Discovery (Lead Identification)

## PATENT STATUS

- **U.S. Patent Filed:** U.S. Patent Application Number 62/685,026 , Filed 14 Jun 2018

## THERAPEUTIC AREA

- Cancer/Neoplasm