

BILE ACIDS AND OTHER AGENTS THAT MODULATE THE GUT MICROBIOME FOR THE TREATMENT OF LIVER CANCER

SUMMARY (1024-CHARACTER LIMIT)

Researchers at the National Cancer Institute (NCI) have discovered that primary bile acids and antibiotics are a novel therapeutic for the treatment of liver cancer and liver metastases. NCI is seeking parties interested in licensing and/or co-developing primary bile acids and antibiotics that have been demonstrated in vivo to attract natural killer T (NKT) cells to the liver and inhibit tumor development.

NIH REFERENCE NUMBER

E-229-2017

PRODUCT TYPE

- Therapeutics

KEYWORDS

- Liver Cancer, Bile Acid, natural killer T Cells, NKT Cells, Greten

COLLABORATION OPPORTUNITY

This invention is available for licensing and co-development.

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STATUS

Active

DESCRIPTION OF TECHNOLOGY

Primary liver tumors and secondary hepatic malignancies are among the leading causes of cancer-related deaths. Liver metastases account for 95% of all hepatic cancers, and the liver is the most common site for organ metastasis in the body. The gut microbiome serves an important role in antitumor immunity regulating the efficacy of chemo- and immunotherapies. The liver is exposed to gut bacteria through blood from the intestine, with 70% of the whole liver's blood supply coming from intestinal blood. Changes in the commensal microbiome may affect immune cell function in the liver. Commensal bacteria have been shown to metabolize primary bile acids to secondary bile acids, and researchers at the

National Cancer Institute (NCI) have found that the balance of primary versus secondary bile acids plays a role in liver cancer development.

Researchers at the NCI have identified a novel mechanism to enhance anti-tumor immunity in the liver by using primary bile acids or antibiotics that increase primary bile acids which attract natural killer T (NKT) cells. Mechanistically, primary bile acid induces the expression of chemokine (C-X-C motif) ligand 16 (CXCL16) on liver sinusoidal endothelial cells leading to an accumulation of C-C chemokine receptor type 6 (CCR6) -positive NKT cells in the liver. The inventors have demonstrated in vivo that primary bile acids or antibiotics increase the accumulation of NKT cells in the liver and decrease the number of liver surface metastases in mice.

The [National Cancer Institute, Thoracic and GI Malignancies Branch](#), is seeking statements of capability or interest from parties interested in licensing this invention and/or collaborative research to further develop, evaluate, or commercialize primary bile acids or antibiotics for the treatment of liver cancer and/or liver metastases.

POTENTIAL COMMERCIAL APPLICATIONS

- Treatment of liver cancer and liver metastases
- Therapeutic use as a combination therapy with immune checkpoint inhibitors and/or chemotherapy

COMPETITIVE ADVANTAGES

- Various formulations of bile acids are already in clinical use and are FDA-approved for the treatment of biliary cirrhosis and bile acid synthesis disorders
- Bile acid formulations and antibiotics are well-tolerated and are biological agents
- Novel anti-tumor function

INVENTOR(S)

[Tim Greten \(NCI\)](#), [Chi Ma \(NCI\)](#)

DEVELOPMENT STAGE

- Pre-clinical (in vivo)

PUBLICATIONS

Ma C, et al. Gut microbiome-mediated bile acid metabolism regulates liver cancer via NKT cells [[PMID 29798856](#)]

PATENT STATUS

- **U.S. Provisional:** U.S. Provisional Patent Application Number 62/578,176 , Filed 27 Oct 2017

RELATED TECHNOLOGIES

- [E-034-2010 - Cancer Therapeutic based on Stimulation of Natural Killer T-cell Anti-tumor Activity](#)

THERAPEUTIC AREA

- Cancer/Neoplasm