NATIONAL CANCER INSTITUTE
Technology Transfer Center

IgG4 Hinge Containing Nanobody-based CARs Targeting GPC3 for Treating Liver Cancer

Summary

Scientists at the National Cancer Institute (NCI) developed a potent chimeric antigen receptor (CAR) targeting glypican-3 (GPC3). GPC3 is a cell surface proteoglycan preferentially expressed on Hepatocellular Carcinoma (HCC). The specific HN3 nanobody-IgG4H-CD28TM CAR included in this invention was much more potent both in in vitro cell models and in vivo mouse models. The NCI seeks licensing and/or co-development research collaborations for further development of the anti-GPC3 CAR to treat liver cancer.

NIH Reference Number

E-205-2021

Product Type

- Therapeutics

Keywords

- Chimeric antigen receptors (CARs), Glypican-3 (GPC3), T Cell, Natural Killer (NK) Cell, Macrophage, Nanobody, IgG4, Therapeutic, Hepatocellular Carcinoma (HCC), Liver Cancer, Cancer Therapeutic, Antibody, Ho

Collaboration Opportunity

This invention is available for licensing and co-development.

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Description of Technology

Hepatocellular carcinoma (HCC) is the most common type of liver cancer. Globally, HCC is the sixth most prevalent cancer and third leading cause of cancer-related morbidity. Standard treatment for HCC is not suitable for a large proportion of liver cancer patients. Part of this is because less than a quarter of HCC patients are surgical candidates for curative-intent treatment. As a result, alternative treatments are needed. Chimeric antigen receptor (CAR) T cell therapy is a promising alternative approach selectively

targets targeting tumors via tumor-specific antigens. However, to date, no effective CAR T cell therapy exists for HCC.

Researchers at National Cancer Institute (NCI) developed novel Chimeric Antigen Receptors (CARs) specific for glypican-3 (GPC3) that include short Immunoglobulin subclass 4 (IgG4) and CD28 based hinge domains and the HN3 human single-domain antibody (also called nanobody). The specific HN3 nanobody-IgG4H-CD28TM CAR included in this invention was much more potent both in in vitro cell models and in vivo mouse models.

Researchers at the NCI seek licensing and/or co-development research collaborations for developing new nanobody-based CAR and/or antibody-T-cell receptor therapies for treating liver cancer.

Potential Commercial Applications

- Treatment of liver cancer, whose worldwide incidence is increasing in direct relation to the spread of hepatitis C virus infection.
- Chimeric antigen receptor (CAR) and/or antibody-T-cell receptor cancer therapies.

Competitive Advantages

- Increased therapeutic effectiveness of CAR T therapies for the vast majority patients with HCC without impactful treatment options
- New nanobody-based CAR immunotherapy in preclinical in vivo studies has a greater decrease in tumor size compared with other CAR formats
- Nanobodies’ lack of a light chain, making them much smaller and more flexible than standard antibodies, allows: (1) binding in different modes than typical antibodies, (2) coverage of more chemical space and (3) binding to epitopes otherwise inaccessible.
- Nanobodies can be readily genetically engineered for additional functionality and, consequently, paths to market.

Inventor(s)

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Development Stage

- Pre-clinical (in vivo)

Publications

Dan Li, et al. Persistent Polyfunctional Chimeric Antigen Receptor T Cells That Target Glypican 3 Eliminate Orthotopic Hepatocellular Carcinomas in Mice. Gastroenterology vol. 158,8 (2020): 2250-2265.e20. doi:10.1053/j.gastro.2020.02.011 [32060001]

Patent Status

- **U.S. Provisional:** U.S. Provisional Patent Application Number 63/277,287, Filed 09 Nov 2021

Related Technologies

- E-130-2011 - Single-domain monoclonal antibodies for the treatment of hepatocellular carcinoma
- E-016-2018 - New Chimeric Antigen Receptor (CAR) Format for Developing Improved Adoptive Cell Therapies

Therapeutic Area

- Cancer/Neoplasm

Updated

Thursday, April 13, 2023

Source URL:https://techtransfer.cancer.gov/availabletechnologies/e-205-2021