NATIONAL CANCER INSTITUTE
Technology Transfer Center

IgG4 Hinge Containing Chimeric Antigen Receptors Targeting Glypican-1 For Treating Solid Tumors

Summary

Researchers at the National Cancer Institute have developed a glypican-1 (GPC1) chimeric antigen receptor (CAR)-T cells using short immunoglobin subclass 4 (IgG4) hinge sequences that are highly potent against GPC1-expressing tumors. NCI seeks research co-development partners and/or licensees to advance the development of GPC1-IgG4 hinge CARs for the treatment of pancreatic cancer and other GPC1-expressing tumors.

NIH Reference Number

E-107-2020

Product Type

- Therapeutics

Keywords

- Glypican-1, GPC-1, Immunoglobulin subclass 4, IgG4, Hinge, Chimeric Antigen Receptor, CAR, Single Domain Antibody, Nanobody, Cancer Therapeutic, Pancreatic Cancer, Ho

Collaboration Opportunity

This invention is available for licensing and co-development.

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Description of Technology

Pancreatic cancer is the fourth most common cause of cancer deaths in the U.S. The overall 5-year survival rate is 8.5%. Glypican-1 (GPC1) is a cell surface heparan sulfate proteoglycan protein overexpressed in pancreatic cancer. Due to preferential expression, GPC1 represents a potential candidate for targeted therapy for pancreatic cancer and other GPC1-expressing cancers, such as prostate.

Researchers at National Cancer Institute (NCI) developed novel Chimeric Antigen Receptors (CARs) specific for GPC1 that include short Immunoglobulin subclass 4 (IgG4) hinge sequences between the extracellular antigen recognition domain and the transmembrane domain. Hinge changes in CAR design can achieve the threshold of

antigen density required for optimal CAR-T cell activity. Significantly, the optimized GPC1-IgG4 hinge CARs have shown rapid and complete tumor regression in mouse models.

Potential Commercial Applications

- Immunotherapeutic applications for the treatment of pancreatic adenocarcinoma – a significant unmet medical need
- Immunotherapeutic applications for the treatment of several GPC1-positive malignancies – including uterine cervical cancer, colorectal cancer, liver cancer, glioma, lung cancer, head and neck cancer, thyroid cancer, endometrial cancer, breast cancer and ovarian cancer

Competitive Advantages

- GPC1-targeted CAR T cells demonstrated potent antitumor efficacy in a peritoneal dissemination xenograft mouse model.
- Recombinant receptors providing both antigen-binding and T-cell–activating functions
- Likely successful targeting and lower toxicity due to high affinity of the GPC1 nanobody fragment
- Incorporation of the IgG4 hinge sequence increases the potency of the nanobody based CARs against pancreatic cancer
- CARs using the IgG4 hinge domain are available for immediate testing
- Potential immunotherapy for several cancer types with few treatment options – including pancreatic adenocarcinoma and uterine cervical cancer

Inventor(s)

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Development Stage

- Pre-clinical (in vivo)

Patent Status

- **PCT:** PCT Application Number 63/065,388 , Filed 13 Aug 2020

Related Technologies

- E-028-2019 - High Affinity Monoclonal Antibodies Targeting Glypican-1

Therapeutic Area

- Cancer/Neoplasm

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