Anti-GPRC5D CAR-T Cell Therapy for Multiple Myeloma

Under Development in Investigator Initiated Trial

Overview

Drug Name	Anti-GPRC5D CAR T-cell
Description	Anti-GPRC5D CAR T-cell is a CAR-T cell therapy targeting G protein-coupled receptor class C group 5 member D (GPRC5D), which is under development in early investigator initiated trial for the treatment of multiple myeloma. The preliminary data from ongoing clinical trial showed astonishing clinical efficacy on relapsed/refractory multiple myeloma (RRMM) patients.
Target	GPRC5D
Drug Modality	CAR-T cell
Indication	Multiple myeloma
Product Category	Cancer immunotherapy
Mechanism of Action	Genetically modified T cells are activated by CARs recognizing GPRC5D to kill multiple myeloma cells
Status	Investigator initiated trial
Patent	Granted

Collaboration Opportunity

Protheragen Inc. is actively seeking partnership for Anti-GPRC5D CAR T-cell. Potential collaboration can be strategic alliance, licensing, or marketing agreement.
We look forward to hearing from you.

Target

GPRC5D

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Introduction	G protein-coupled receptor class C group 5 member D (GPRC5D) is an orphan G protein-coupled receptor whose function in human tissues is still unclear. This receptor is expressed in several myeloma cell lines and bone marrow plasma cells from patients with multiple myeloma. In normal tissues, substantial GPRC5D expression is limited to plasma cells, and low expression is in a subset of cells in hair follicles and hard keratosis tissues.
Approved Name	G protein-coupled receptor class C group 5 member D
Official Symbol	GPRC5D
Gene Type	Gene with protein product
Synonyms	G protein-coupled receptor, family C, group 5, member D
Ensembl	ENSG00000111291
Gene ID	55507
mRNA Refseq	NM_018654.2
Protein Refseq	NP_061124.1
OMIM	607437
UniProt ID	Q9NZD1
Chromosome Location	12p13.1

Clinical Resources

Gene Function	The protein encoded by this gene is a member of the G protein-coupled receptor family. However, the specific function of this gene has not been determined.
Major Conditions	Multiple myeloma

Drug Modality

CAR-T Cell

Based on a multi-pass transmembrane protein production and purification platform, a single B cell platform for rapid and accurate isolation of positive antibody sequences, and an antibody humanization platform, Anti-GPRC5D CAR T-cell with high specificity, high affinity, and high cytotoxicity was developed.

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Indication

Multiple Myeloma

Multiple myeloma, also known as myeloma, is a B cell-dependent hematological malignancy caused by excessive clonal proliferation of terminally differentiated plasma cells in bone marrow. Characteristic features of myeloma include surplus plasma cells in the bone marrow and extramedullary sites, elevated monoclonal M-protein in serum and urine, osteolytic bone lesions, renal insufficiency, anemia, and immunodeficiency. According to Globocan consulted in 2018, the age-standardized incidence rate of multiple myeloma on a global scale is 1.5 per 100,000. Approximately 153,000 new cases of multiple myeloma were diagnosed worldwide in 2017, according to the Global Burden of Disease study. Current treatments for multiple myeloma include drug therapy, radiation therapy, autologous bone marrow transplantation, and supportive care. Patients should be ideally treated on an individualized basis according to a risk-adapted approach that balances efficacy with potential side effects.
The introduction of many new drugs has dramatically changed the outcome of multiple myeloma patients. But despite a significant improvement in overall survival, multiple myeloma remains largely incurable due to the resistant and refractory nature of the disease.

Mechanism of Action

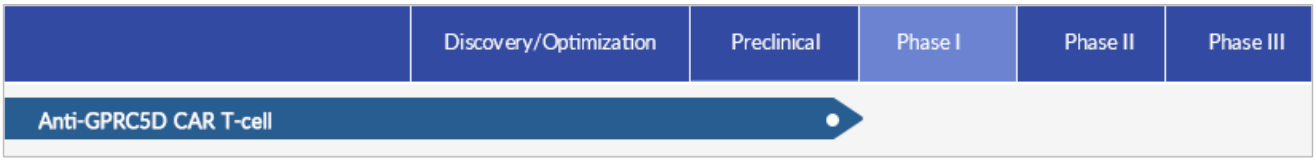
Genetically Modified T Cells Activated by CAR Targeting GPRC5D to Kill Multiple Myeloma Cells

GPRC5D is expressed on malignant bone marrow plasma cells, whereas normal tissue expression is limited to the hair follicles and eccrine glands. GPRC5D has been identified as an immunotherapeutic target in multiple myeloma with small potential for undesired targeted/off-tumor effects.
Anti-GPRC5D CAR T-cell is a CAR-T cell therapy that targets GPRC5D for the treatment of multiple myeloma. When the CAR specifically binds to GPRC5D on the multiple myeloma cells, the T cell is activated through signal transduction. Activated CAR-T cells kill tumor cells through several mechanisms, including extensive stimulated cell proliferation, increased degree of cytotoxicity, and increased secretion of factors to affect other

cells, such as cytokines, interleukins, and growth factors.

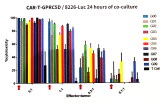
Status

The Status of Anti-GPRC5D CAR T-cell



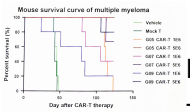
Data

In Vitro Tumor Cell Cytotoxicity Assay



The experimental data showed that several CARs constructed by proprietary technology platforms exhibited stronger cytotoxic capacity compared to bench-mark CAR (G00), especially at low effector to tumor cell ratios.

In Vivo Antitumor Effects in A Mice Model



Multiple myeloma model mice infused with two dosages of three candidate anti-GPRC5D CAR-T cells exhibited elongated survival time comparing with control groups.

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