

NEXT GENERATION ALLOGENEIC CAR-NK CELL PLATFORM FOR TREATMENT OF MALIGNANT DISEASES

Keywords: CAR-NK, NK cells, CD44v6, CEA, breast cancer, colon cancer, pancreatic cancer, leukemia

INVENTION NOVELTY

This innovative platform offers "off-the-shelf" CAR-NK cells with extensive applicability against solid tumors and hematological cancers. The resulting cell products are designed to overcome significant limitations of current engineered cellular immunotherapies in cancer, such as immunosuppressive tumor microenvironment and side effects.

VALUE PROPOSITION

The recent development of cellular therapeutics using CAR-T cells represents a significant breakthrough in cancer care. This therapy has been highly successful in CD19+ leukemia and lymphomas, but has been largely ineffective in other malignancies, especially solid tumors. Currently, major obstacles preventing broader applicability include tumor stroma-related immunosuppression, cytokine release syndrome, and high production costs. The innovative platform has two major features to address these obstacles: 1) second-generation CAR constructs incorporating elements to enhance anti-tumor activity and to overcome immunosuppression in the tumor microenvironment (TME), and 2) iPS-derived NK cells as effector cells for the generation of an allogeneic "off-the-shelf" product. NK cells exhibit a favorable safety profile compared to T cells due to a significantly reduced risk for GvHD. They can be used as an allogeneic treatment and can be produced in large numbers and stored as an "off-the-shelf" product.

TECHNOLOGY DESCRIPTION

The platform is based on a characterised and verified iPSC cell line with an integrated CAR vector to produce CAR-NK cells. CAR integration is performed by non-viral transfection, avoiding the high costs associated with the use of viral vectors. The current lead construct targets CD44v6 and incorporates an IL-15 superagonist as a strategy to enhance anti-tumor activity and a checkpoint inhibitor component since, like in T cells, PD-1 is a critical negative regulator of NK cells. CD44v6 has been implicated in tumorigenesis, tumor cell invasion, and metastasis. It is expressed in lymphomas, leukemias, solid tumors, and is present in the majority of breast cancers. The first indication for a clinical phase I/IIa will be Acute Myeloid Leukemia (AML). CD44v6-Specific CAR-NK cells have demonstrated effective cytotoxicity against CD44v6 expressing cell lines such as triple-negative breast cancer (TNBC) cell lines. Efficacy is also shown in 3D spheroid models to demonstrate the potential for solid tumors. The pipeline of cell products from the platform includes products against pancreatic cancer, triple-negative breast cancer, and glioblastoma. The project is developed in the research group of Prof. Dr. Gabriele Pecher (Head of the Competence Center Immuno-Oncology and Translational Cell Therapy), embedded at the Charité University Hospital with infrastructure including laboratories, patient access, GMP facility, and a clinical study center. The project is seeking collaborations with industrial partners, including options for licensing.

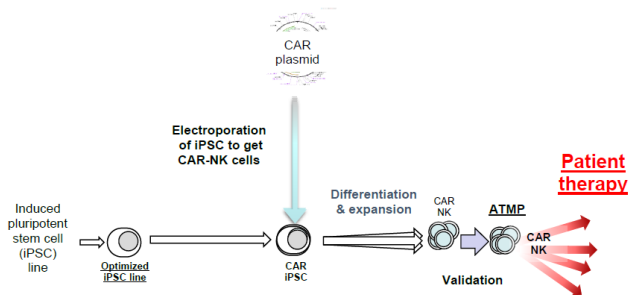


Figure Platform Technology

DEVELOPMENT STATUS

Currently TRL 3.

COMMERCIAL OPPORTUNITY

Licensing or collaboration for further development.

PATENT SITUATION

Patent applications in EP, US, JP and AU originating from PCT patent applications WO2022043312 and WO2022043315 with priority date 24.8.2020.