Non-Viral, Non-Integrating DNA Vectors for the Safe and Efficient Engineering of Primary Human Cells

Keywords

- Safe, persistent and efficient genetic modification
- Only clinically approved components
- Applications include immunotherapy, stem cell therapy, and biotechnology

Abstract

This technology utilizes a novel DNA Vector platform for the safe and efficient generation of genetically engineered cells. This DNA vector system contains no viral components and comprises only clinically approved sequences, which makes it ideal for applications for human therapy such as immuno- and stem-cell therapy.

Development Stage

Convincing preclinical data has shown that the system produces stably transfected cells *in vitro* and *in vivo* in which the expression of transgenes is persistently sustained at high levels without decline in primary human T-Cells, stem cells and cancer cell lines. We have demonstrated that our DNA Vectors can genetically modify T-Cells to express transgenic Chimeric Antigen Receptors and T-Cell Receptors without adversely affecting their viability. Most importantly we demonstrate that these modified cells can efficiently target and kill human cancer cells *in vitro* and in mouse models as effectively as currently used clinically applied viral vectors.

The Technology

The system is based on an S/MAR element. It does not integrate into target cells' genomes and it replicates autonomously and extrachromosomally in the nucleus of all dividing eukaryotic cells.

Applications and Commercial Opportunity

The applications span all areas of genetic engineering. In particular this system is a safer technology for the introduction of T-Cell receptors or Chimeric Antigen Receptor into naive Human T-Cells that can be used for autologous immunotherapy.

There are currently over 300 clinical trials in this area. In the majority of these trials the genetic modification of the cells is achieved using a randomly integrating systems such as lentivirus or transposons. Immunogenicity and the risk of genotoxicity associated with their random genomic integration still represent a fundamental limitation of these systems.

Our technology, on the other hand, avoids the risk of integrative mutagenesis and the potential for the reactivation of endogenous viruses or transposons. Additionally, no other vector of this class is capable of providing the efficiency, cost-effectiveness and persistence of transgene expression in dividing primary cells of this vector system.

Inventors

The investigators are Dr. Matthias Bozza & Dr. Richard Harbottle.

Intellectual Property

Priority application EP 17191829.5 was submitted on 19.09.2017.

Further Information

No other public information is currently available, but further information is available under a signed Confidential Disclosure Agreement (CDA).

DKFZ Contact:

For further information, including a CDA, please contact:

Lana Semykina
Deutsches Krebsforschungszentrum
Technology Transfer Office T010
Email: s.semykina@dkfz.de
Tel.: +49-(0)6221-42-2953