



mRNA structure for protein expression

mRNA structure for protein expression



Patent title	mRNA structure for protein expression, and use thereof	Inventor	Korea Research Institute of Bioscience and Biotechnology / Kim Tae-don
Patent application No.	KR 10-2019-0152938 (PCT/KR2020/016988)	Authority status	Unpublished

Technicality

Technology overview

- An mRNA structure comprises ① a region for encoding a protein or a peptide, ② a 5'-β-globin UTR region at the upstream of the protein encoding region, and ③ a BGH, BGH-IRES, or IRES-BGH region at the downstream of the protein encoding region.
- An mRNA or mRNA structure of the present invention improves the intracellular expression or expression stability of a chimeric antigen receptor or a chimeric antigen receptor protein, improves the intracellular persistence, enhances the stability of a chimeric antigen receptor in a body, and improves the killing ability of cancer cells. Thus, the structure can be usefully utilized for the anticancer pharmaceutical composition and the anticancer immunotherapy targeting solid cancer.

Development background and problem to be solved

- Transgenic CAR-CAR-NK cells using DNA have a problem in which stability is not guaranteed because a CAR gene is integrated into a genome or mutation occurs.
- To solve this problem, attempts have been made to use transiently transformed CAR-NK cells, but in the case of transient transformation using mRNA, there were no studies showing results due to mRNA instability and low transfection rates and target protein expression rates.

Excellence and discrimination of technology

Excellence of technology

- Protein expression and persistence of an mRNA structure increase.
- The expression rate of a CAR protein increases.
- Anticancer efficacy of CAR-NK increases.
- mRNA stability increases, and in vivo stability is secured.

Discrimination of technology

- Protein expression increases and mRNA stability is enhanced by a gene combination of an mRNA untranslated region (UTR).
- When an mRNA structure technology is applied to the expression of a CAR gene, the amount and persistence of expression increase. Thus, the anticancer efficacy of CAR-NK is enhanced.
- As an mRNA structure capable of expressing various proteins, the mRNA structure can be used as a universal vehicle for a gene treatment agent.

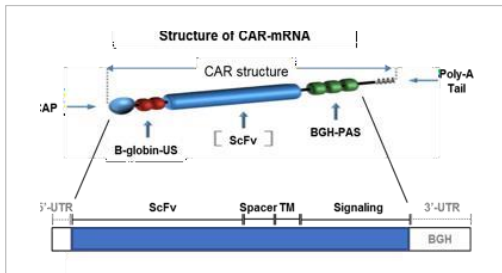


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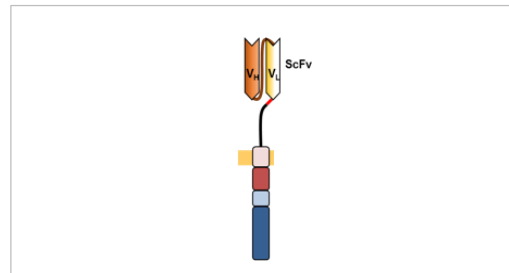
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Implementation method

- An mRNA structure technology is applied to the expression of CAR genes to increase the amount and persistence of expression.
- Protein expression increases and mRNA stability increases by a gene combination of an untranslated region (mRNA UTR).
- The intracellular expression or expression stability and intracellular persistence of a chimeric antigen receptor or chimeric antigen receptor protein (CAR protein) are enhanced. Also, the in vivo stability of a CAR protein is enhanced. Thus, the technology is utilized for the anticancer pharmaceutical composition and the anticancer immunotherapy targeting solid cancer.



Picture 1 CAR-mRNA structure



Picture 2 CAR-mRNA structure

Degree of technology completion (TRL)

Degree of technology completion: TRL4 (Lab Scale prototype development stage)

TRL1	TRL2	TRL3	TRL4	TRL5	TRL6	TRL7	TRL8	TRL9
Technical principle presentation	Technology concept setting	Technology concept verification	Lab Scale prototype development	Implementation environment application experiment	Full Scale prototype development	Quasi-commercial product development	Commercial product development	Commercial product implementation

Utilization

Utilization field and applied product

Utilization field

- Vaccine industry
- Antibody treatment agent industry
- Anticancer agent industry



Vaccine Antibody treatment agent Immune cell treatment agent

Picture 1 Anticancer immunotherapy

<Data: National Cancer Information Center >

Applied product

- RNA vaccine
- Antibody treatment agent
- Immune cell treatment agent
- Universal vehicle



Picture 2 Immunooncology

<Data: MSD, BMS>



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Technology trend

- A new immunotherapy has been developed. A chimeric antigen receptor (CAR) which reacts specifically with cancer cells is artificially introduced into T cells or NK cells by using a genetic recombination technology and is cultured in vitro at a high concentration. Then, the same is injected back into a cancer patient to enhance an immune response with respect to cancer cells and ultimately kill the cancer cells.
- Since 2010, the results of clinical trials using CAR-T cells as a treatment agent have been published one after another. In 2017, Novartis' CAR-T treatment agent "Kimriah" was approved for sales by the US FDA as a treatment agent for acute lymphoblastic leukemia patients for the first time in the world.
- Compared to CAR-T, CAR-NK is being developed relatively late.
- Currently, startups such as Fate Therapeutics, Nkartra Therapeutics, and NantKwest are active in the United States to develop CAR-NK treatment agents.
- In Korea, CAR-NK is being developed by Green Cross Lab Cell and Korea Research Institute of Bioscience and Biotechnology.

Family patent status

Application nation	Application No. (Application date) / Registration No.	Title of the invention
KOR	KR 10-2019-0152938 /-	mRNA structure for protein expression, and use thereof

Market prospect

Target market size and prospect

- The global vaccine market size is expected to reach USD 103.57 billion by 2028, growing at a CAGR of 11% from USD 33.57 billion in 2017.
- With the rapid aging of the population, an increase in infectious diseases, and the advent of blockbuster vaccines, profitability of the industry is enhanced. Also, new research and production technologies, new financing opportunities, and the like promote the growth of the global vaccine market.

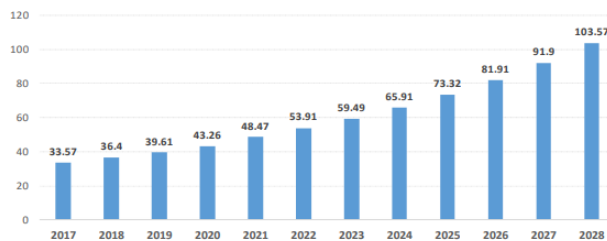


Table Global vaccine market status and prospect [billion dollar]

<Data: Biotech Policy Research Center >



Picture Global vaccine market share by companies, 2017

<Data: Biotech Policy Research Center >

Technology transfer query

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Technology transfer process

