News Release

Successful Development of CAR-T Cell Therapy Targeting Eva1 of Solid Tumors

Key Points

- We have successfully developed a CAR-T cell therapy targeting solid tumors.
- By optimizing the CAR-T cell structure—such as the spacer length and intracellular domains—we improved the therapeutic effects both in vitro and in vivo.
- The humanized CAR-T cells targeting Eva1 (MPZL2), named Eva1CAR-T, showed strong antitumor effects in mouse models of lung cancer and pancreatic cancer.

Summary

A research group led by Dr. Masahide Osaki (1st author), Dr. Shiho Hirano, Lecturer Seitaro Terakura (Correspondence), and Professor Hitoshi Kiyoi from the Department of Hematology and Oncology, Nagoya University Graduate School of Medicine, in collaboration with Assistant Professor (Special Appointment) Masaki Sunagawa, Associate Professor Toshio Kokuryo, and Professor Tomoki Ebata from the Department of Surgical Oncology, Nagoya University Graduate School of Medicine, and the company CURED Inc., has successfully developed a chimeric antigen receptor (CAR)-T cell therapy targeting Eva1 (MPZL2), an antigen widely expressed in solid tumors.

While CAR-T cell therapies targeting CD19 or BCMA have already been applied clinically for hematologic malignancies such as leukemia and malignant lymphoma, their application to solid tumors has not yet been realized. In this study, the researchers focused on Eva1, which is strongly expressed in several solid tumors including lung and pancreatic cancer, and designed and optimized a CAR structure based on a humanized anti-Eva1 antibody. CAR-T cells with a short spacer region and intracellular domains of 4-1BB or CD79A/CD40 showed excellent antitumor effects against cancer cells.

Additionally, they evaluated the expression of Eva1 on normal monocytes and quantitatively analyzed the antigen density threshold for CAR-T cell response from a safety perspective. The results indicated that these Eva1CAR-T cells

could potentially respond effectively to tumor cells while minimizing excessive reaction to normal cells.
This Eva1CAR-T cell therapy is expected to be a promising new immunotherapy for solid tumors.
The results of this research were published online in the international journal *Journal for ImmunoTherapy of Cancer* on May 8, 2025.

Research Background

In recent years, chimeric antigen receptor T cell (CAR-T) therapy—where T cells are genetically modified to recognize specific cancer cells—has demonstrated remarkable therapeutic effects in patients with refractory hematologic malignancies, and its clinical application is rapidly progressing. CAR-T cells targeting antigens such as CD19 and BCMA, which are specific to hematologic cancers, have shown high response rates in relapsed/refractory B cell malignancies. CD19-CAR-T and BCMA-CAR-T therapies are now commercially available and have achieved significant clinical success.

In contrast, CAR-T cell therapy for solid tumors has not yet been realized in clinical practice. One of the main reasons is the lack of ideal target antigens that are expressed on tumor cells but not on normal tissues. Moreover, several other factors hinder the efficacy of CAR-T therapy in solid tumors, including the difficulty of T cell infiltration into the tumor site, the presence of immunosuppressive tumor microenvironments, and T cell exhaustion.

This research group focused on Eva1 (MPZL2), a protein known to be highly expressed in several solid tumors such as lung cancer, pancreatic cancer, hepatocellular carcinoma, and bladder cancer. Eva1 has been reported to be involved in tumor growth and metastasis. Furthermore, Eva1 is a small-sized membrane protein, which may facilitate effective immunological synapse formation when recognized by T lymphocytes on the cell surface—potentially enhancing CAR-T cell activation efficiency. Based on these characteristics, the aim of this study was to develop and optimize CAR-T cells targeting Eva1.

Research Results

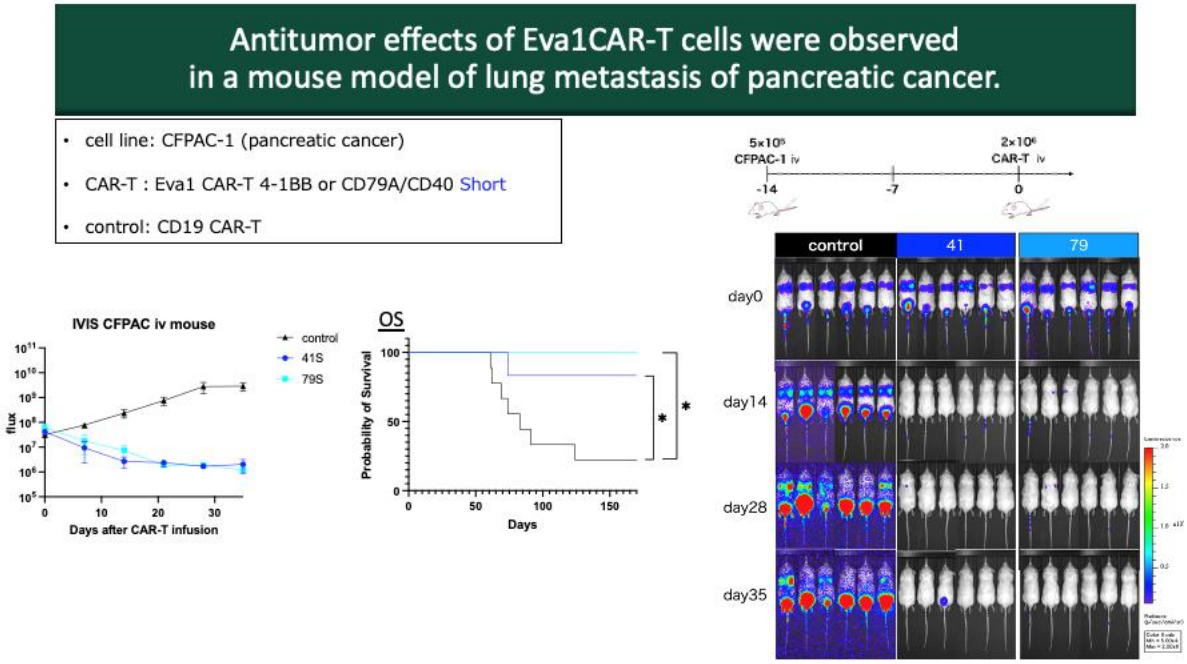
In this study, the researchers humanized a mouse-derived anti-Eva1 antibody

and screened 16 humanized antibody candidates to identify a sequence that demonstrated both high specificity for the cancer antigen and the ability to induce T cell proliferation. They then created multiple CAR constructs by combining different spacer lengths (which determine the distance between the antigen and T lymphocyte) and intracellular signaling domains (CD28, 4-1BB, or CD79A/CD40, which enhance intracellular T cell signaling), in order to determine the optimal configuration.

As a result, Eva1CAR-T cells incorporating a short spacer region and either a 4-1BB or CD79A/CD40 intracellular domain exhibited superior antitumor efficacy in both in vitro and in vivo experiments. Notably, in mouse models using lung cancer (NCI-H1975) and pancreatic cancer (CFPAC-1) cell lines, complete tumor regression was achieved with a small number of administered CAR-T cells ($1–2 \times 10^6$ cells).

On the other hand, because weak expression of Eva1 was also observed in normal monocytes, the team conducted safety evaluations to assess how CAR-T cells distinguish between normal and cancerous cells. The analysis revealed that effective antigen recognition and cytokine production occurred only when the antigen density of Eva1 was high. This suggests the potential to avoid excessive responses against Eva1-low normal tissues, thereby improving safety.

These findings indicate that Eva1-targeting CAR-T cells may serve as a new therapeutic option for solid tumors, representing a significant step toward clinical application.



Research Summary and Future Perspective

The Eva1CAR-T cells developed in this study open up new possibilities for CAR-T therapy against solid tumors, which has long been considered challenging.

Future studies will focus on further evaluating the reactivity of these CAR-T cells to normal tissues and confirming their safety in humans, with the goal of clinical translation.

Since Eva1 is expressed in various types of cancer cells, the potential application of Eva1CAR-T therapy may be expanded to multiple types of solid tumors.

Publication

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