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Company Name: HEALIOS K.K.
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(TSE Mothers Code: 4593)

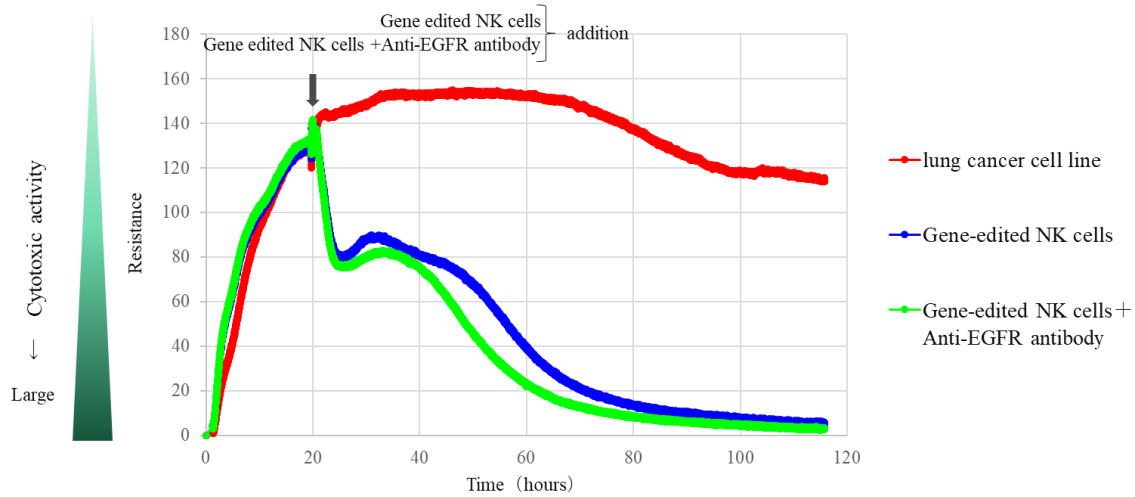
The anti-tumor effect of Healios' gene edited iPSC-derived NK cells in a lung cancer cell line

HEALIOS K.K. (“Healios”) has been researching and developing next-generation cancer immunotherapies for solid tumors*¹ using NK cells*² derived from allogeneic iPSCs whose specific functions have been enhanced with gene editing technology (development code: HLCN061). Although solid tumors account for the vast majority of cancer deaths, there is currently no available immunotherapy for patients impacted by this disease and it represents one of today’s greatest unmet medical needs. As part of its effort to address this need, Healios has successfully edited the genes of iPSCs and differentiated these into NK cells with certain functional enhancements resulting from the gene editing (“gene edited NK cells”).

We are pleased to announce that the gene edited NK cells have demonstrated a robust *in vitro* anti-tumor (cytotoxic) effect on a lung cancer cell line (A549, non-small cell lung cancer). Their cytotoxic activity was determined by measuring the change in electrical resistance resulting from the addition of the NK cells, as illustrated in the below chart. In addition to testing the gene edited NK cells alone against the cancer line, we also tested the gene edited NK cells in combination with an anti-EGFR antibody used as an anti-cancer drug, which resulted in enhanced cancer cytotoxicity. In both cases, a decrease in electrical resistance almost to the baseline after around 80 hours was observed, suggesting significant cellular damage to the cancer cell line.

[Research Results]

***In vitro* anti-tumor effect of gene edited NK cells in a lung cancer cell line**



At the same time, we have released new videos showing the cytotoxic effect of the gene edited NK cells on a cancer cell spheroid created from a lung cancer cell line, which confirms that the gene edited NK cells attacked and killed the cancer. Please watch the videos in the following links for more information.

Video 1: Effect of Healios' gene edited NK cells on a lung cancer cell spheroid

(https://youtu.be/uIJ0BtkI_hA)

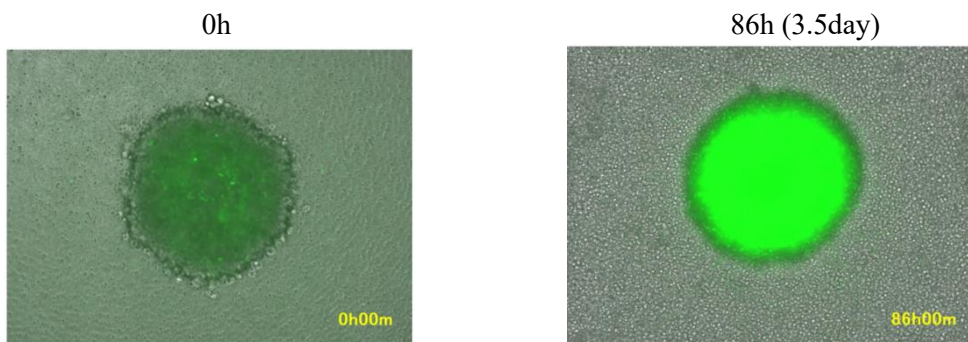
Video 2: Effect of anti-EGFR antibody on a lung cancer cell spheroid

(https://youtu.be/A7cXdKb7O_w)

Video 3: Combination effect of Healios' gene edited NK cells and an anti-EGFR antibody on a lung cancer cell spheroid (<https://youtu.be/rPs9b7-KrKE>)

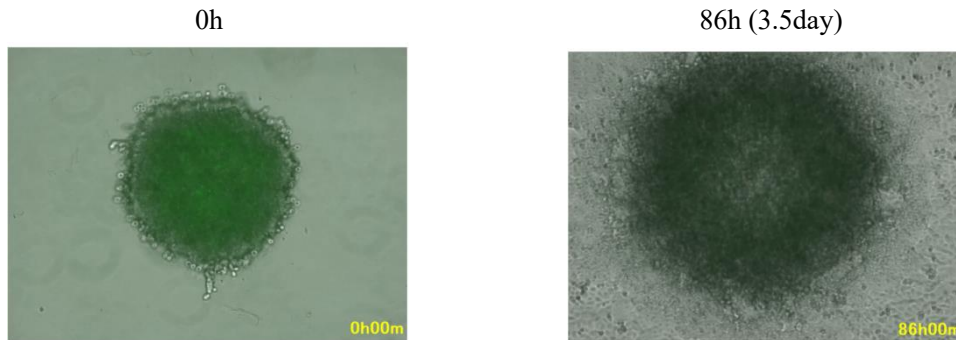
[Reference: Video]

Video 1: Progress after adding gene edited NK cells



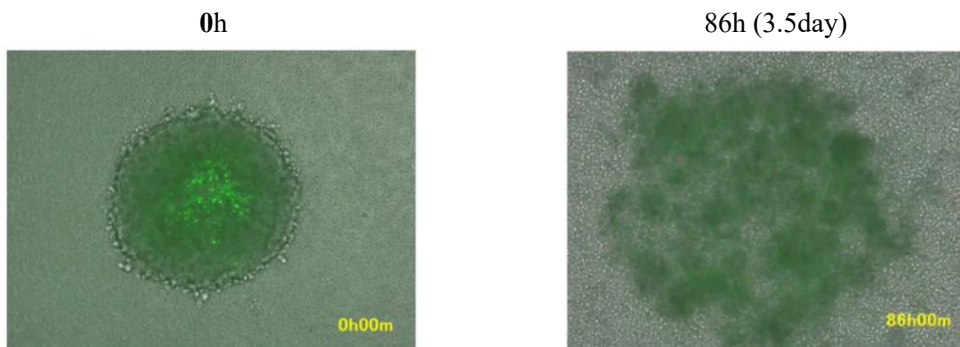
Gene edited NK cells have killed the cancer cells (the marker glows green when cell death is detected).

Video 2: Progress 0h - 86h (3.5 days) after adding anti-EGFR antibody alone



The cancer cells survived and the cancer cell spheroid expanded for 86 hours with the anti-EGFR antibody alone.

Video 3: Progress 0h - 86h (3.5 days) after adding gene edited NK cells + anti-EGFR antibody



By combining gene edited NK cells and the anti-EGFR antibody, the lung cancer cells were efficiently killed and the lung cancer cell spheroid was destroyed. The combination of gene edited NK cells and antibody treatments may be an effective approach to addressing difficult to treat solid cancers.

While the advent of molecular-targeted drugs and cancer immunotherapy has improved the treatment outcome for cancer patients, solid cancer remains a disease without effective therapeutic options. Healios will continue to accelerate its research and development activities aimed at delivering effective gene edited iPSC-derived NK cells for solid tumor patients.

*1 Solid tumors

A general term for cancers that form in organs and tissues other than blood cancers.

*2 Natural killer (NK) cells

Natural killer (NK) cells are a subset of lymphocytes, a type of white blood cell. NK cells play

a central role in a cell mediated defense system that human bodies naturally have, and attack cancer cells and virus-infected cells. The expected efficacy of treatments using NK cells includes life-extension, promotion of healing, relief of symptoms, and improvement of quality of life.

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