1336 Verification of the effect of human allogeneic iPS cell-derived gene-engineered NK cells (eNK ® cells HLCN061) on mesothelioma

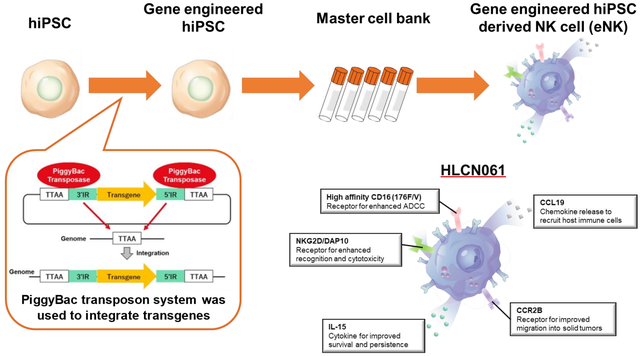
Seiji Matsumoto[1)], Yoshiko Fujita[1)], Kumiko Goto[2)], Yuka Sato[2)], Fusako Nishigaki[2)], Yasuyuki Higashi[2)], Hironobu Kimura[2)], Kouichi Tamura[2)]

1) Department of Thoracic Surgery, Hyogo Medical University, Japan

2) HEALIOS K.K., Japan

Background

Malignant pleural mesothelioma is a malignant tumor that is caused by exposure to asbestos. Because it is a rare cancer, there are few drugs that can be used to treat it. Healios is developing iPSC-derived NK cells (eNK cells) (HLCN061) engineered with NKG2D, DAP10, IL-15, CD16, CCL19, and CCR2B genes for the treatment of refractory solid tumors. This study evaluated the antitumor effect of eNK cells against human malignant pleural mesothelioma cell lines.



Methods

The antitumor effect of eNK cells on human malignant pleural mesothelioma cell lines in vitro was evaluated using the Viability/Cytotoxicity Multiplex Assay Kit (WST-8/LDH).
In vivo, immunodeficient mice were subcutaneously inoculated with human malignant pleural mesothelioma cell lines. After subcutaneous tumor formation, eNK cells were inoculated into or near the tumor, the size of the subcutaneous tumor was measured, and the tumor volume was compared with that of an untreated group. After the study was completed, the tumors were removed and the tumors in the untreated group and the eNK cell-administered group were analyzed using RNA-seq.

Results

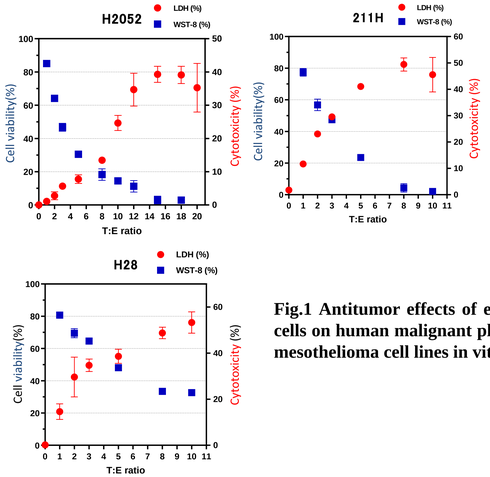


Fig.1 Antitumor effects of eNK® cells on human malignant pleural mesothelioma cell lines in vitro.

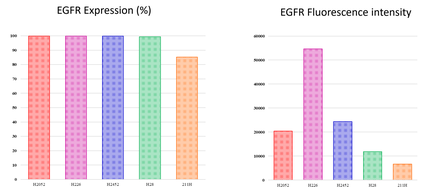


Fig.2 Expression of EGFR on mesothelioma cell lines
All human malignant pleural mesothelioma cell lines express EGFR, H226 has the highest expression intensity

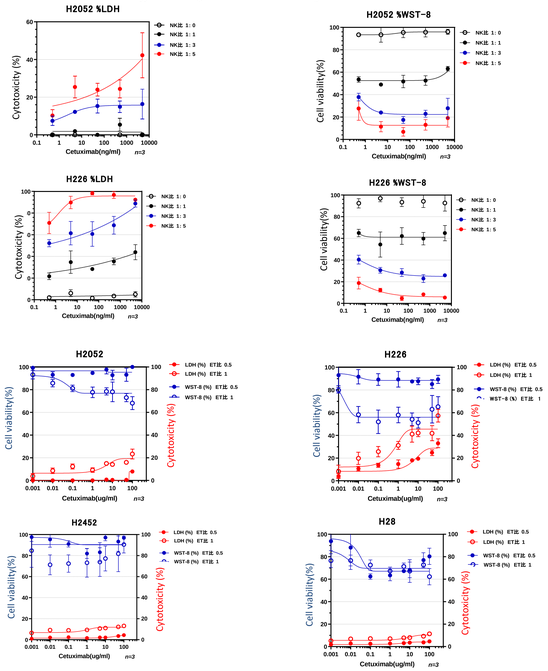


Fig.3 The combination of eNK ® cells and anti-EGFR antibody (cetuximab)
In H226, which has the highest EGFR expression intensity, the combination of eNK ® cells and anti-EGFR antibody (cetuximab) in H226, which has the highest EGFR expression intensity.

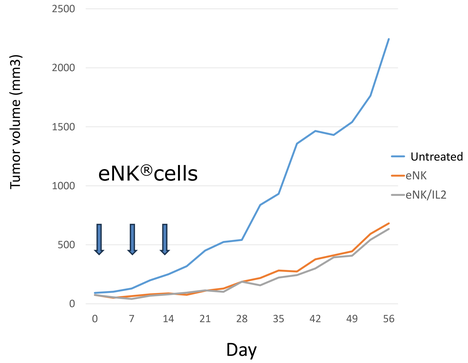


Fig.4 Antitumor effects of eNK® cells on human malignant pleural mesothelioma cell lines (H226) in vivo

eNK® cells 1x10^{7}cells/dose intratumorally 3 times weekly (near tumor administration)
Intraperitoneal administration of 5 μg/dose of IL-2 for 0-4 weeks, 5 days/week in the IL-2 group
eNK ® cells with or without IL-2 treatment inhibited subcutaneous tumor growth

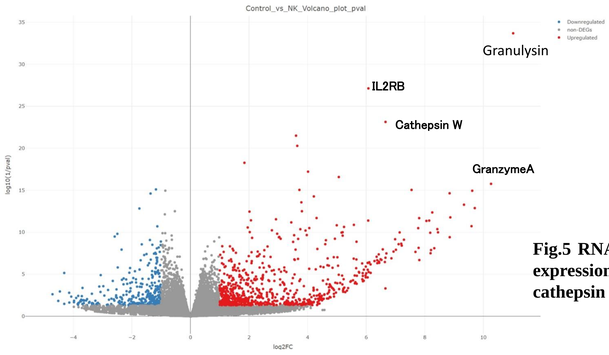


Fig.5 RNA-seq showed increased expression of granulysin, IL2RB, cathepsin W

Conclusions

The antitumor effect of eNK cells against human malignant pleural mesothelioma cell lines was confirmed in vitro. In a mouse subcutaneous tumor model, the eNK cell treatment group suppressed tumor growth compared to the untreated group ($p \leqq 0.05$). RNA-seq showed increased expression of granulysin, IL2RB, cathepsin W, etc. in subcutaneous tumors treated with eNK cells.

Corresponding author: Seiji Matsumoto
smatumo@hyo-med.ac.jp

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