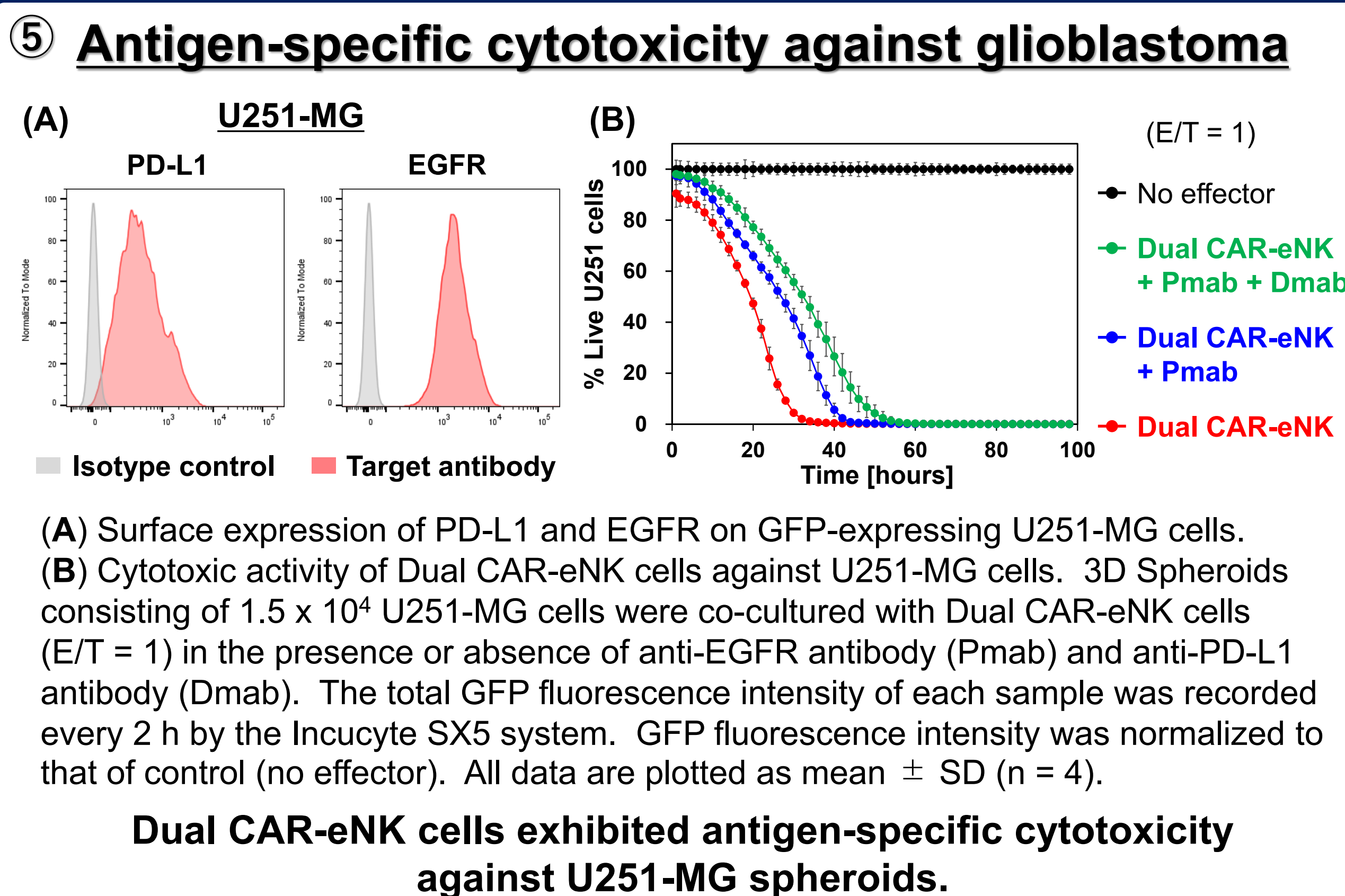
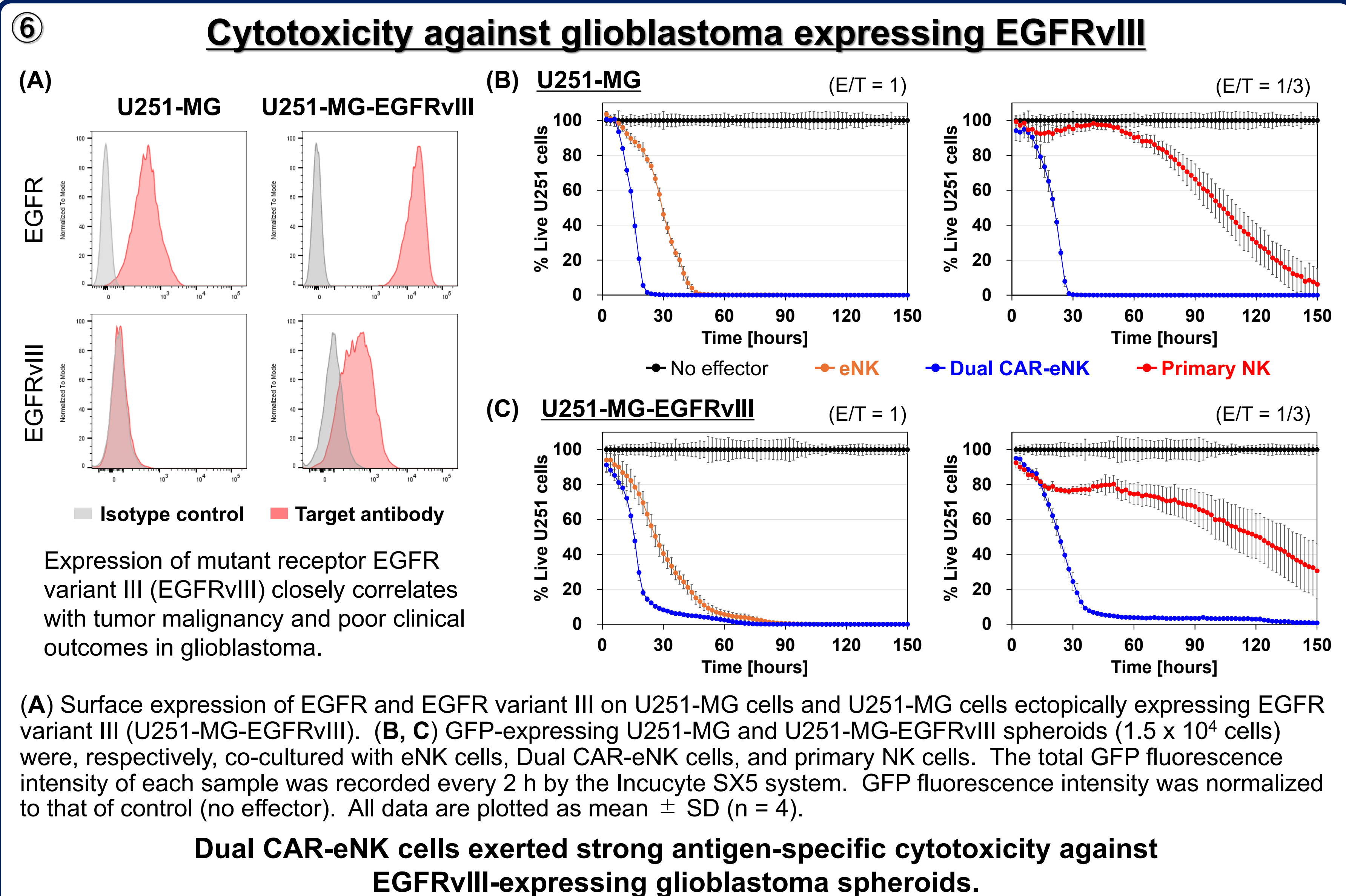
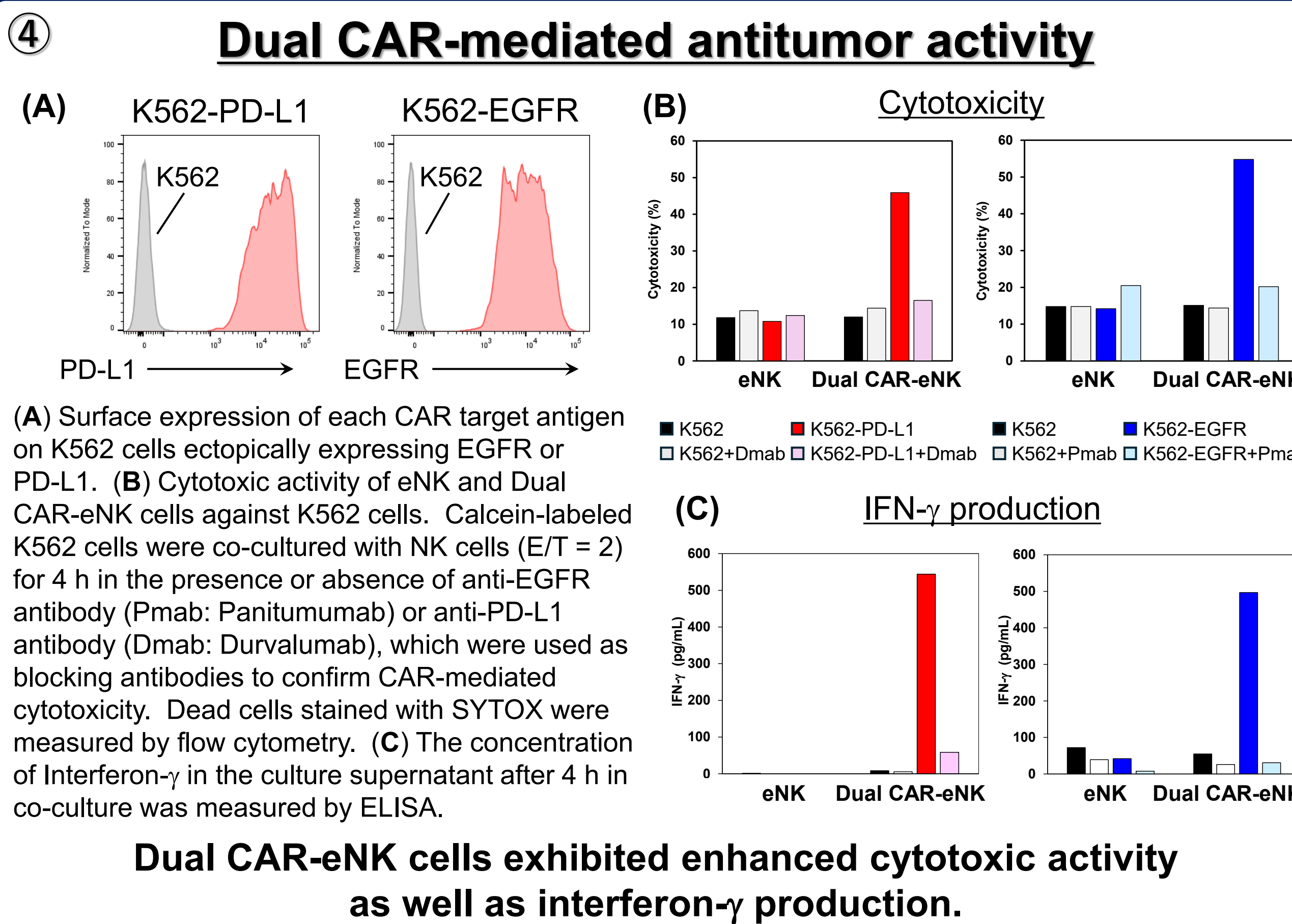
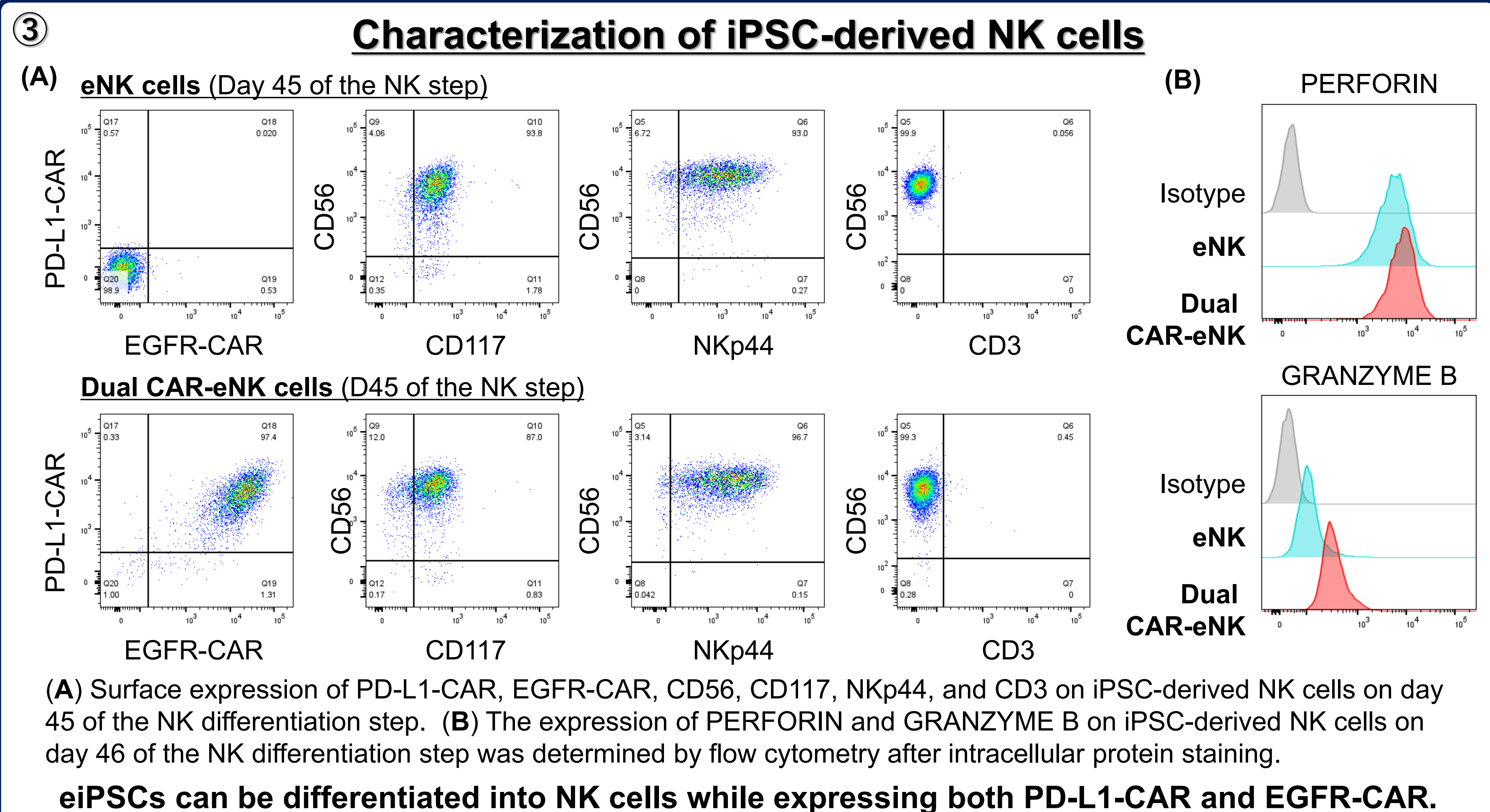
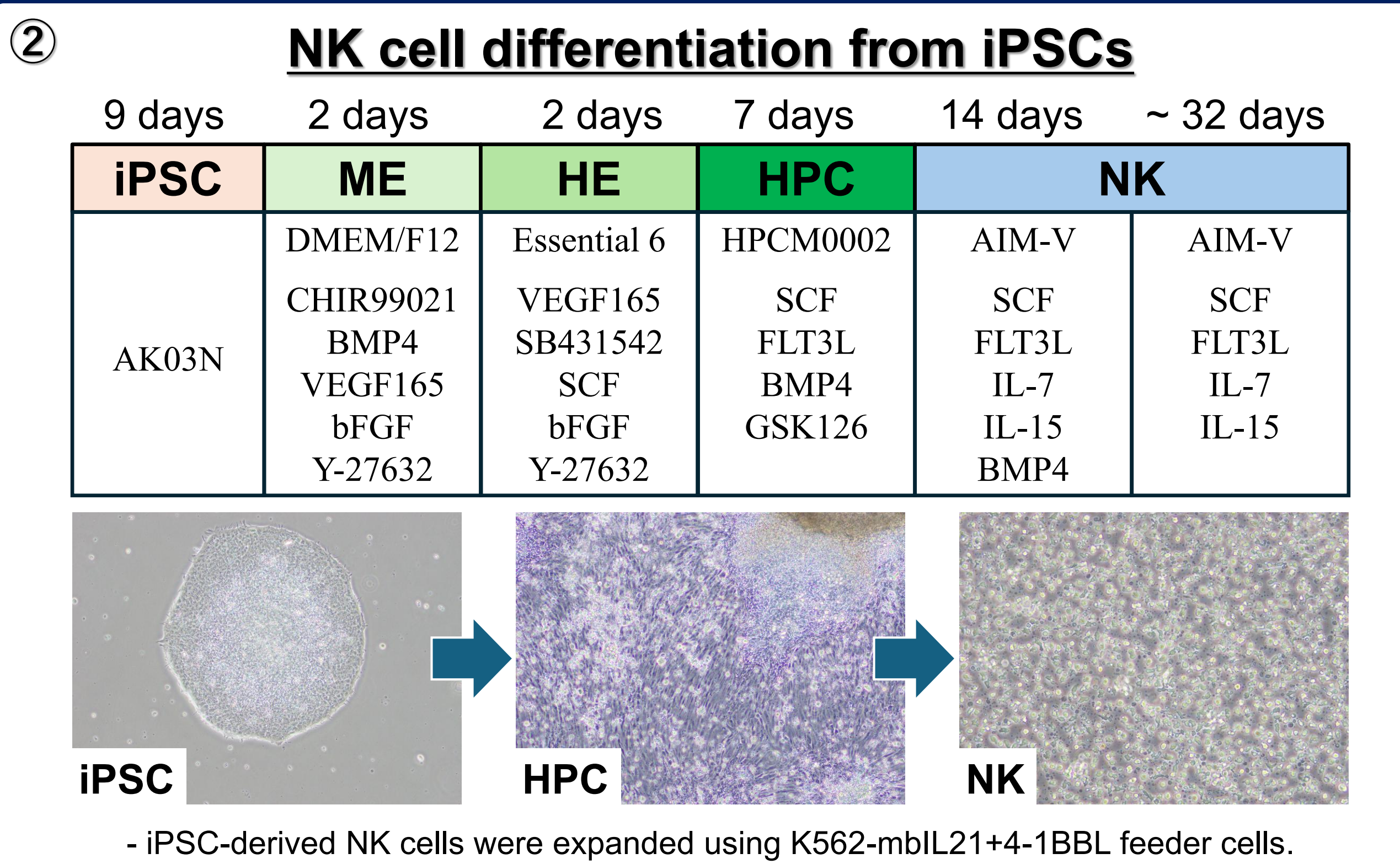
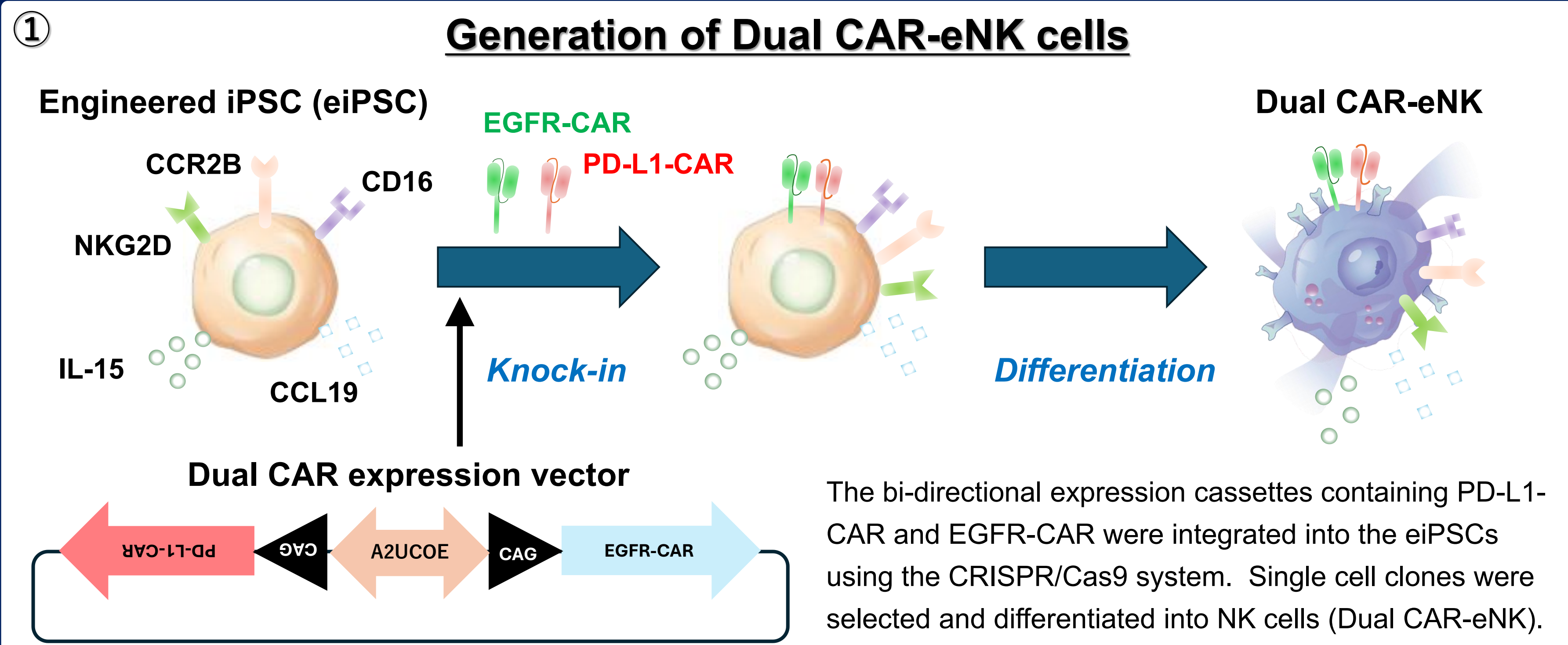


# Engineered human iPSC-derived dual CAR-NK cells targeting EGFR and PD-L1 for glioblastoma

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**Glioblastoma (GBM)** is the most common and aggressive primary brain cancer with a very poor prognosis and limited therapeutic options. Here, we used iPSC cells to produce gene-engineered natural killer (NK) cells equipped with chimeric antigen receptors (CARs) to treat GBM. We have previously developed engineered NK (eNK) cells derived from human iPSC cells (eiPSCs) which are genetically engineered to express IL-15, CCR2B, CCL19, high-affinity CD16, and NKG2D/DAP10 complex. The eNK cells demonstrated improvement of survival, persistence, tumor infiltration, and immune cell recruitment, as well as high cytotoxicity against tumor spheroids<sup>1,2</sup>. In the present study, we further enhanced antitumor activity of the eNK cells by expressing dual CARs targeting epidermal growth factor receptor (EGFR) and programmed death-ligand 1 (PD-L1), which are highly expressed on GBM, and whose expression correlates with poor prognosis. We demonstrate that Dual CAR-eNK cells can exert strong antigen-specific cytotoxicity against GBM spheroids. Therefore, Dual CAR-eNK cells have the potential to provide a novel strategy for GBM therapy.



**Conclusion**

- We established Dual CAR-eNK cells stably co-express both PD-L1-CAR and EGFR-CAR.
- Dual CAR-eNK cells exhibited enhanced cytotoxic activity as well as interferon- $\gamma$  production against cancer cells expressing target antigens.
- Dual CAR-eNK cells exerted strong antigen-specific cytotoxicity against EGFRvIII-expressing glioblastoma spheroids.
- Dual CAR-eNK cells did not elicit antigen-specific cytotoxicity against non-malignant human astrocytes.

**Dual CAR-eNK cells offer a novel strategy for GBM therapy.**

References: (1) Fukutani Y. et al., *Stem Cell Res. Ther.*, 16, 373 (2025).  
(2) Sato Y. et al., *Cancer Immunol. Immunother.*, 74, 129 (2026).

