

HATAIWAN KUNKANJANAWAN : EFFECTS OF LPS AND YHHU-3792 ON THE
EXPANSION OF NATURAL KILLER CELLS DERIVED FROM HUMAN UMBILICAL CORD
BLOOD. THESIS ADVISOR : ASSOC. PROF. RANGSUN PARNPAI, Ph.D., 58 PP.

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CORD BLOOD-DERIVED NATURAL KILLER CELLS

Adoptive cell transfer of *ex vivo* expanded natural killer (NK) cells holds significant hope in cancer immunotherapy. However, some points of using NK cells in cancer treatment include source of NK cells, conditions for their expansion, resulting number and purity of NK cells after culturing, and anti-cancer activity of the expanded cells need to be considered. To establish a sustainable supply of NK cells for clinical applications, this study has developed a feeder-free and cell sorting-free method for expanding cord blood-derived NK (CBNK) cells. By stimulating cord blood derived mononuclear cells (CB-MNCs) with Lipopolysaccharide (LPS, 1 ug/mL) during the first week of expansion, this study demonstrates that the presence of LPS triggered a significant increase in CBNK cell proportions ($P<0.01$). Further upscaling of the expansion reveals that, from a single cord blood unit, the proposed procedure results in an average of $1.68\pm 2.92\times 10^{10}$ total nucleated cells (TNCs), of which $92.09\pm 3.47\%$ of the expanded cells are NK cells. Results from flow cytometry analysis showed that the expanded CBNK cells were co-positive with various NK cell markers: CD16 ($83.63\pm 8.27\%$), NKG2D ($98.33\pm 1.55\%$), NKp30 ($73.42\pm 17.55\%$), NKp44 ($36.74\pm 11.12\%$), and NKG2A ($73.92\pm 12.09\%$). Moreover, the anti-cancer activities of the expanded CBNK cells were investigated in K562, MIA PaCa-2, and SKOV3 cells; each serving as a representative cancer cell model for chronic myeloid leukemia, pancreatic carcinoma, and ovarian carcinoma, respectively. After 4 hours of co-incubation, more than 50% specific lysis was observed at effector to target cell ratios as low as 3.125:1 in all tested models. Collectively, these results illustrate that the proposed feeder-free and cell-sorting-free expansion method can effectively yield clinically relevant doses of purified CBNK cells with intact functions.

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Student's Signature Hat.
Advisor's Signature Parnpai