

# T cell immunobiology and immunomodulation

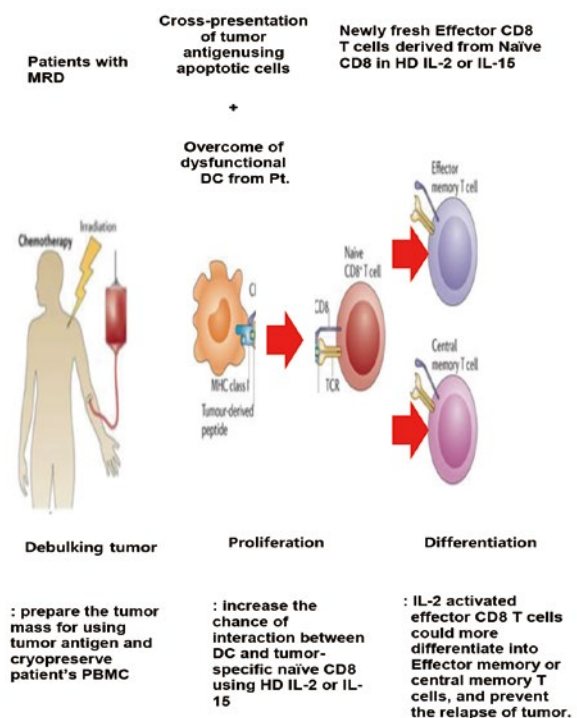
## Major Research aims

For the purpose of increasing the therapeutic effect in adoptive T cell therapy, the generation of potent tumor-specific cytotoxic CD8 T cells is essential for cancer immunotherapy. Primary effector T cells derived from naive CD8 T cells are expected to have potent CTL function without exhaustion or terminally differentiation compared to secondary effector from memory T cells. However, it is the main key factor that how can increase the limited number of tumor-specific naïve CD8 T cells by thymic negative selection during the development of T lymphocytes.

## Major achievements

1. Successful expansion of human CD8<sup>+</sup> naïve, memory and TILs *in vitro and different* Exhaustion phenotypes of in vitro-generated different sources of effector cells
2. Expression of transcription factors T-bet and Eomesodermin in CD8<sup>+</sup> effector cells and assessment of foxp1 expression differences
3. Generation of tumor-specific CTLs from naïve CD8 T cells by IL-2 priming

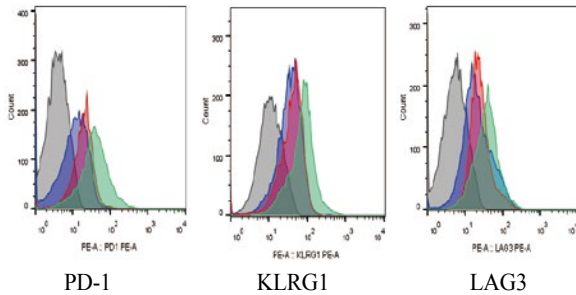
4. Achievement of excellent study grant from Korean Government in 2016



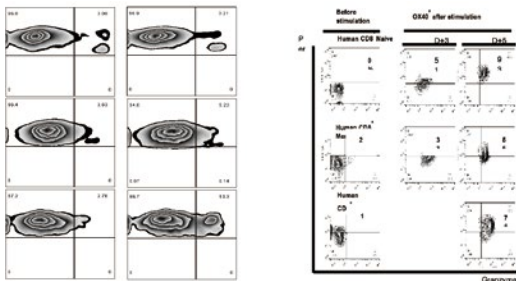
## Representative figures of major achievements

1. Effector cells (NT<sub>eff</sub>) derived from naïve cells after stimulation with anti CD3/CD28 dynabeads and

anti-CD2 for 5 days, expressed lower levels of the exhaustion markers, such as PD1, CTLA4, KLRG1, or LAG3 compared to effector cells (MT<sup>eff</sup> or TIL<sup>eff</sup>) from memory or CD8<sup>+</sup> TILs(A) in human



2. Annexin V/PI assay by flow cytometry. Quadrant plots showed the percentage distribution of cells including early and late apoptotic cells(Right) with or without 48-hour exposure of TGF- $\beta$  and in vitro analysis of cytokine production from three effectors. NT<sup>eff</sup> demonstrated significant increase of perforin<sup>+</sup> granzyme B<sup>+</sup> portion compared to MT<sup>eff</sup> and TIL<sup>eff</sup> at two time points



## Major relevant publications

1. Nguyen HH, Kim T, Song SY et al. Naïve CD8(+) T cell derived tumor-specific cytotoxic effectors as a potential remedy for overcoming TGF- $\beta$  immunosuppression in the tumor microenvironment. *Sci Reports* 16(6) 2016
2. Yhim HY, Kim JS, Mun YC et al. Clinical Outcomes and Prognostic Factors of Up-Front Autologous Stem Cell Transplantation in Patients with Extranodal Natural Killer/T Cell Lymphoma. *Biol Blood Marrow Transplant.* 2015 May 8.
3. Jung SH, Ahn JS, Kim YK et al. Prognostic significance of interim PET/CT based on visual, SUV-based, and MTV-based assessment in the treatment of peripheral T-cell lymphoma. *BMC Cancer.* 2015 Mar 28;15:198

## Contact information

Deok-Hwan Yang, M.D., Ph.D.

Department of Hematology-Oncology

Tel: 82-61-379-7636 Fax: 82-61-379-7628

E-mail: drydh1685@hotmail.com