Effective conditioning regimen in adoptive T cell therapy of cancer

Chungyong Han

National Cancer Center, Korea

Adoptive T cell therapy (ACT), a strategy for cancer treatment, has shown impressive therapeutic potential in hematologic cancer and melanoma. The strategy involves administration of tumor-reactive T cells such as T cells engineered with chimeric antigen receptor and the T cell receptor (TCR). Lymphodepletion pre-conditioning, which is generally performed before the T cell infusion, enhances the efficacy of ACT by increasing the graft rate of the T cells. However, the function of the transferred T cells is affected by immune-suppressive cells that repopulate after lymphodepletion. We designed a post-conditioning regimen that involves transient treatment with CD4-depleting antibody. In ACT of murine melanoma, the combination of cyclophosphamide pre-conditioning and anti-CD4 post-conditioning significantly enhanced anti-tumor efficacy. The combination regimen accelerated the expansion of CD8+ T cells and increased the proportion of IL-18Rα-high T cell subset which induced strong anti-tumor immune response in an IL-18/TCR signaling dependent manner. This study demonstrates the clinical relevance of anti-CD4 post-conditioning in ACT and provides insights into the function of IL-18Rα-high CD8+ T cells in cancer immunology.