세미나 초록

성명	이승우
소속	POSTECH
발표 주제	Cancer Immunotherapy by T cell Engager Antibody
발표 내용	Bispecific T cell engagers (TCEs) show promising clinical efficacy in blood tumors, but their application to solid tumors remains challenging. Fc-fused IL-7 (rhIL-7-hyFc, efineptakin alfa) is a long-acting form of recombinant human IL-7 and is currently under clinical trials for various cancers in combination with immune checkpoint inhibitors. Here, we show that rhIL-7-hyFc changes the intratumoral CD8 T cell landscape, enhancing the efficacy of TCE-immunotherapy. rhIL-7-hyFc induces a dramatic increase in CD8 tumor-infiltrating lymphocytes (TILs) in various solid tumors, but the majority of these cells are PD-1-negative tumor non-responsive bystander T cells. However, they are non-exhausted and central memory-phenotype CD8 T cells with high TCR-recall capacity. To redirect IL-7-primed bystander TILs to kill tumor cells, we use TCEs composed of two single-chain variable fragments simultaneously targeting CD3ε and tumor antigens, including PD-L1 and HER2. With TCR activation by TCEs, bystander CD8 T cells gain cytotoxic activity to tumor cells. In addition, we observe the antitumor response of IL-7-primed bystander CD8 T cells when redirected in vivo by TCE in RAG1-/- mice. Consequently, the combination of rhIL-7-hyFc and TCE enhances the antitumor responses by upregulating CD8 TILs. Single-cell transcriptome analysis reveals that rhIL-7-hyFc-induced bystander CD8 TILs transform into cycling transitional T cells by TCE-redirection with decreased memory markers and increased cytotoxic molecules. Notably, TCE treatment has no major effect on tumor-reactive CD8 TILs. Our results suggest that rhIL-7-hyFc treatment promotes the antitumor efficacy of TCE-immunotherapy by increasing TCE-sensitive bystander CD8 TILs in solid tumors.