

Novel Reporter System Monitoring IL-18 Specific Signaling can be Applied to High-Throughput Screening

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Very recently, the immunotherapies against cancer, autoimmune diseases, and infection have been feasible and promising. Thus, we have examined the possibility whether or not human gamma delta T cells can be applied for the novel immunotherapies. We previously established the cells stably maintaining NFκB-driven human secreted embryonic alkaline phosphatase (SEAP) expression. The cells can be used to determine the transcription activity of NFκB with high-standard dynamic range and accuracy. Because IL-18 is a kind of cytokines that enhances cytotoxicity and activity of human gamma delta T cells through NFκB activation, we have focused on the activity and signaling of IL-18. In this study, we modified the previous reporter cell that can determine the transcription activity of NFκB to express two subunits consisted of human IL-18 receptor. The modified cells secreted SEAP in response to treatment with human recombinant IL-18 in a concentration-dependent manner. We also observed the concentration-dependently enhancement of NFκB activity in the cells treated with mouse recombinant IL-18 although the affinity was lower compared to human recombinant IL-18. We also previously established the cells stably expressing and secreting human recombinant IL-18 and then validated whether or not the conditioned medium from the cells activate NFκB transcription activity using this assay. We demonstrated drug screening using number of extracts derived from marine bacteria and synthetic compounds.