Секция «Клеточная биология и гистология»

Natural Killer Cells Cytotoxic Activity In The Presence Of IL-15 And IL-18

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NK cells were originally described as cytolytic effector lymphocytes, that exhibit cytotoxic activity towards altered cells. Quality of NK cells cytotoxicity depends on the cytokine microenvironme Interleukin 18 is an immunostimulatory cytokine that contributes to NK cell migration, and primes murine NK cells for proliferation by promoting protein synthesis, survival, and autophagy [2]. Interleukin 15 enhances cytotoxicity, receptor expression, and expansion of neonatal natural killer cells [1]. Aim was to evaluate the effect of preculturing NK cells with IL-18 and IL-15 on cells' cytotoxic function.

In this study, we use NK cells of NK-92 cellular line and target cells of chronic myelogenous leukemia K562 cellular line. NK-92 cells were precultured for 24h separately with IL-18 or IL-15 at concentrations of 10ng/1ml and 1ng/1ml, respectively. Next day, NK-92 cells were added to 96-well plate, target cells K562 cells were treated with 2,7μM CFSE solution and placed into the wells of 96-well plate at a ratio of 5:1 effector:target. After incubation for 4h, the cells were stained by 2μl/ml PI solution. Evaluation of NK-92 cytotoxic effect was performed using FACSCantoII flow cytometer (BD, USA). The data were processed using Statistica 10.0 software. The Mann—Whitney U test was used for comparison of the obtained results. The differences were significant at ($p<0.05$).

NK cells of the NK-92 cellular line had a cytotoxic effect on K562 cells. The relative number of K562 dead cells increased when co-culture with NK-92 cells, compared with base death. The cytotoxic effect of NK-92 cells was increased in the presence of IL-18 and IL-15, compared to NK-92 cells cytotoxic effect without IL-18 or IL-15 ($p<0.0001$).

Our findings ensure that NK cells of the NK-92 cellular line have cytotoxic effect towards K562 cells, and this effect is enhanced by preculturing NK-92 cells with each of IL-18 and IL-15. IL-18 rapidly activates NF-κB and regulates various cellular processes such as gene transcription, protein synthesis that can enhance the cytotoxic effect of NK cells. IL-15 induces AKT phosphorylation and this leads to activate transcription of many genes that positively regulated the cytolytic activity of NK cells. Possibly the mechanism of NK cells cytotoxic activity change after preculture with IL-18 and IL-15, is related to these signaling molecules activity.

Funding: Nsh-2873.2018.7

References

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