Enhanced cytotoxic effect of NK-92 cells toward K562 target cells in the presence of propeptide dipeptides of granzymes A and B

P-02.3-11

I. Dolenc[I], J. Božič[I]

[I]Jozef Stefan Institute, Ljubljana, Slovenia

Cathepsin C (dipeptidyl-peptidase I) activates granzymes A and B by proteolytic removal of their N-terminal dipeptides. The possible physiological role of the cleaved dipeptides Glu-Lys and Gly-Glu is not yet understood. Our research showed that adding either of the two dipeptides to NK-92 cells resulted in enhanced cytotoxicity toward the targeted K562 cells and increased death rate of the target cells. Cathepsin C is known to generate cytotoxic polymers from various dipeptides, as seen for Leu-Leu-OMe. However, in the case of the dipeptides Glu-Lys and Gly-Glu, cathepsin C was unable to polymerize them. We showed that the enhanced cytotoxicity in the presence of the dipeptides is perforin depended. Additionally, the dipeptides were found to be inhibitors of the transferase activity of cathepsin C (IC50 < 20 mM), and weak competitive inhibitors of the peptidase activity with Ki values in the millimolar range.