Abstract

Acute myeloid leukemia makes up for 18 % of all leukemias among pediatric and young adult patients. The complete remission rate (80-90 %) and the overall survival (70 %) of the patients is relatively high, nevertheless, the relapse rate is still almost at 50 % and the prognosis remains extremely bad. The relapse treatment is rather challenging because the persisting leukemic clones might in fact start to be refractory to chemotherapy. Lately, NK cells are being perceived as an attractive therapeutical tool for treatment of the relapses. NK cells are a subpopulation of innate lymphoid cells, possessing the ability to eliminate dysfunctional cells through cytotoxic activities and further perpetuate the immune response. One of the advantages of NK cells is their functional independency of specific antigens. In the light of growing evidence about the role of leukemic stem cells in context of acute myeloid leukemia, NK cells seem to offer a new perspective in therapeutical efforts to eliminate them via several cytotoxic mechanisms. Yet despite optimistic preliminary results, treating this disease has proved to be rather challenging and the NK cell-based immunotherapy is still facing several limitations. Transforming growth factor β is partially responsible for maintenance of leukemic stem cell populations and impairment of NK cell-mediated immune response. The overall negative effect of transforming growth factor β on NK cells was confirmed by functional cytotoxic assays, as well as analysis of expression. In time-dependent manner, transforming growth factor β exposure led to decrease of cytotoxic potential of NK cells and caused dysregulation in expression of several key molecules, such as activating receptors, metabolic regulators and other molecules related to NK cell migration. The effects of long-term transforming growth factor β-induced suppression were reversed by inhibitors, suggesting that administration of the right medication following the adoptive transfer could protect the NK cells in the patient.

Key words: acute myeloid leukemia, AML, bone marrow, NK cell, suppressive microenvironment, transforming growth factor β, TGF-β, cytotoxicity 3