ABSTRACT

Therapy by monoclonal antibody to CD34 molecule

Growth-inhibitory and proapoptotic effect of the monoclonal antibody to CD34 molecule, clone 4H11, were tested on CD34+ leukemic cell lines (MOLM-9, JURL-MK1) and CD34- cell line (PS-1). We have found that the monoclonal antibody to CD34 inhibited the proliferation and induced apoptosis of all CD34+ cell lines tested, however it has similar effect on CD34- leukemic cell line (PS-1) in concentration higher than 32 μg/ml. We did not observe induction of differentiation by anti-CD34 antibody, but a growth arrest of cells in the G0/G1 phase of the cell cycle was detected in CD34+ cell lines. Combinations of anti-CD34 antibody with both type I (α, β) or type II (γ) interferons did not enhance the effects on the cell growth or inhibition of cellular proliferation of the antibody alone. Combinations of anti-CD34 antibody with hematopoietic cytokines or INF-γ did not induced diferentiation. Our data suggest that the monoclonal antibody to CD34 molecule prepared from clone 4H11, after sufficient experimental and preclinical testing on laboratory animals, may provide a new basis for possible targeted antibody therapy of acute or chronic myeloid leukemia.

Therapy by histone deacetylase inhibitors

Histone deacetylase inhibitors (HDACi) are emerging new class of anticancer agents that act by inhibiting cell growth, inducing cell cycle arrest and apoptosis of various cancer cells. However, in some conditions, apoptosis can be blocked and non apoptotic cell death and irreversible growth arrest, namely senescence, can be activated as potential tumor-suppressor mechanism. Here we evaluated the dosage effects of HDAC inhibitors suberoylanilide hydroxamic acid (SAHA) and valproic acid (VPA) in a series of human leukaemia cell lines. We investigated, what concentration of SAHA and VPA can induce apoptosis, growth inhibition or stress-induced premature senescence. We have found that inhibition of proliferation and induction of apoptosis by the treatment with SAHA or VPA is variable depending on the dose, time of the treatment, and on the cell type. The senescence phenotype was preferentially induced by lower dosage of HDACi and required longer incubation time (5 days) while apoptosis was induced by higher dosage and appeared already after 48 h.