

Hematopoiesis is a process of blood cells production and maturation. All disturbances in the normal process of hematopoiesis, leads to hematopoietic and lymphatic system tumor formation, including development of leukemia and lymphoma. A characteristic of these diseases, is blocking of blood cells growth and differentiation to mature and fully functional form. Every year in Poland leukemia and lymphoma affects about 6 thousand people. In adults, the disease is of approx. 5%, while in children at approx. 50% of all malignancies. Treatment of these diseases are difficult and in most cases they are incurable. The molecular mechanisms responsible for their development is still unknown. It is known that chemotherapy is toxic to normal cells of the body, so scientists started to look for substances which would be able to inhibit tumor growth and unlock the differentiation process. The 80s of the twentieth century was the biggest breakthrough in the search for these kind of substances. To date, the only example of successful differentiation therapy is the use of all-trans retinoic acid (ATRA). However, ATRA causes frequent remission of acute promyelocytic leukemia (APL) by inducing the promyelocyte differentiation. Vitamin D<sub>3</sub> (calcitriol) was also noted to induce leukemia cell differentiation in the M1 murine myeloid cell line. The issue of hypercalcemia, which occurs when the concentrations of calcitriol greatly exceed the physiological range and has previously limited its clinical applications can be addressed by the dual strategy of developing analogs of calcitriol with reduced calcium mobilizing properties, and combining these with other compounds that enhance the differentiation-inducing actions of calcitriol or its analogs. One such analogue is tacalcitol (PRI-2191), used as a drug for hyperproliferative disorders, like psoriasis. Biological effects of calcitriol is elicited by the binding to vitamin D receptor (VDR). The high expression of vitamin D receptor in tumor cells is beneficial prognostic and reduces the risk of death. Also, the intracellular concentration of calcitriol is determined by CYP24. However, the mechanism of action of vitamin D<sub>3</sub> in the process of cell differentiation is still unknown. Growing evidence confirmed that tiny structures called microRNAs (miRNAs) may be responsible for failure to use curative therapies. MiRNAs have the ability to block a number of intracellular molecules, such as receptor for vitamin D and CYP24. It is believed that differences in calcitriol action may result, from changes in the intracellular concentration of calcitriol, vitamin D receptor and CYP24, which are blocked by the miRNA. Proposed studies will represent a huge increase in knowledge of mechanisms responsible for differentiation process under the influence of vitamin D<sub>3</sub>. It would also enable the molecular identification of a factor that could be the potential target for anticancer therapy. Therefore, studies aiming analysis of possible molecules/factors that can serve for appropriate patients selection and/or served as additional targets improving effectiveness of therapy are of interest.