**Summary**

***The molecular factors determining sensitivity of human leukemia and lymphoma cells***

***to calcitriol and tacalcitol***

The aim of this study was understanding the differences in the sensitivity of human leukemia and lymphoma cells to the antiproliferative activity of calcitriol and tacalcitol. We evaluated the effect of these substances on nine myeloid and lymphoid cell lines, and then examined whether the sensitivity was dependent on linear origin, cell differentiation, the presence of aneuploid cells, cell cycle and cell cycle regulatory proteins, the number of receptors responsible for biological activity of tested substances, polymorphism of the classic vitamin D receptor and miRNA molecules that can both directly and indirectly affect the sensitivity of human leukemia and lymphoma cells to the use of calcitriol and tacalcitol.

The results of the study indicate that the sensitivity of human leukemia and lymphomas cells to calcitriol and tacalcitol is dependent on cell origin and cell differentiation. Myeloid cells were more sensitive than lymphoid cells. Also, the presence of chromosomal translocation associated with aggressive disease, apoptosis resistance and fusion proteins, increased the sensitivity of leukemia and lymphoma cells to calcitriol and tacalcitol. Similarly, the presence of aneuploid cells was associated with increased proliferation inhibition by tested substances. Calcitriol and tacalcitol increase level of differentiation antigens such as CD11b and CD14 and induces autophagy in sensitive cells. The level of two receptors binding calcitriol and tacalcitol: vitamin D receptor –VDR and 1,25D3-MARRS increased only in leukemia-sensitive cells.The presence of the FokI polymorphism responsible for the formation of two forms of the vitamin D -VDR receptor protein and the "baT" haplotype were characteristic for calcitriol and tacalcitol sensitive cells. Also, p53 status may be responsible for cell sensitivity, as wild type of p53 were observed in sensitive cells, compare to unsensitive cells which contain mutant p53 protein. The studies suggested that two miRNAs miR-27 and miR-125b may play a key role in the activity of calcitriol and tacalcitol in the cells by decreasing the vitamin D-VDR receptor, p53 protein and NFκB transcription factor level. However, to confirm this suggestion further studies are needed.

These studies suggest that the sensitivity of human leukemia and lymphomas cells is not determined by one molecular factor, but is a result of the interaction of several molecular factors present in the cell.