

Regulation of the *VDR* gene expression during murine hematopoiesis.

Abstract:

Vitamin D₃ shows a wide range of biological activities related to the functioning of the calcium-phosphate metabolism and the proper functioning of the immune system. The activity of vitamin D₃ is related to the activation of the nuclear receptor, which belongs to the group of steroid receptors. The vitamin D receptor is responsible for the control of the expression of many genes. Moreover, the latest research indicates a connection between the level of this receptor expression and the prognosis in patients with acute myeloid leukaemia. The anticancer effect of vitamin D₃, which is related to the activity of its intracellular receptor, is based on the activation of the process of the cancer cells differentiation. Nowadays, the influence of VDR signalling on leukemic cells is widely known, but its importance in the process of the normal haematopoiesis still remains obscure. The research confirms the presence of this receptor in blood cells, but its importance and function have not been fully understood. The method of regulating the expression of the VDR gene in the process of haematopoiesis is also unknown.

The aim of the research was to learn about the mechanisms responsible for the regulation of the vitamin D receptor gene expression in the process of haematopoiesis. The experiment was carried out on the mouse research model which is the most widely used model for research into human haematopoiesis. In the process of the research, the promoter of the VDR gene used in blood cells was identified. The 5' end variants and the VDR gene transcription starting points were determined. The VDR gene expression profile in mouse blood cells was determined, and the obtained results confirmed the hypothesis that transcriptionally active VDR is present not only in differentiated blood cells, but also in hematopoietic stem and progenitor cells. The promoter methylation pattern of the examined gene was determined and the regulatory factors responsible for binding of the VDR within the VDR locus were established.

The obtained results enable a comparative analysis of the regulatory mechanisms characteristic of the normal hematopoietic cells with the data on cancer cells, which consequently may enable the determination which of the observed phenomena constitute the physiological norm and which indicate the initiation of cancer processes in blood cells.