

## STRESZCZENIE W JEZYKU ANGIELSKIM

**Title:** The role of NKT-like cells in endocrine system

**Introduction:** The immune and endocrine systems form an interconnected network in which hormones, cytokines, and effector cells interact in multiple directions, both directly and indirectly. Increasing scientific evidence confirms the presence of hormonal receptors, such as the thyroid-stimulating hormone receptor (TSHR) and the vitamin D receptor (VDR), on the surface of immune cells, including T and B lymphocytes, monocytes, dendritic cells (DC), and Natural Killer cells (NK). These data confirm that endocrine factors have an important role in modulating the immune response, which is relevant to the pathogenesis of autoimmune diseases, cancers, and infectious diseases. Natural Killer-T like cells (NKT-like) form a unique population that links innate and adaptive immunity and can rapidly produce cytokines and cytotoxic proteins. Due to their ability to modulate inflammatory responses, these cells constitute an important aim of research on the mechanisms integrating immune and endocrine system functions. The assessment of hormonal and metabolic factors influencing the distribution of NKT-like cell subpopulations in human peripheral blood represents a significant step toward understanding the interrelationship between endocrine and immune systems and may contribute to the development of new diagnostic and therapeutic strategies in clinical medicine.

**Aim:** The purpose of the presented series of articles was to analyze the expression of TSHR on the surface of NKT cells and to assess hormonal and metabolic factors modulating the distribution of NKT-like cell subpopulations. The studies aimed to expand the knowledge on role of the interactions between endocrine and immune systems in regulation of function of these cells.

**Materials and Methods:** The analysis included patients diagnosed at the Department of Endocrinology and Metabolic Diseases and in an outpatient clinic for benign thyroid nodules between 2022 and 2024. Peripheral blood mononuclear cells (PBMCs) were isolated using the gradient method from all the participants, followed by identification of NKT-like cells and their subpopulations by a flow cytometry (FC) method. In the first study, which analyzed TSHR expression, the results were additionally verified using transverse transcription polymerase chain reaction (RT-PCR) method, performed on leukocyte–platelet buffy coats obtained from healthy blood donors. The levels of glucose, total calcium, and vitamin D were determined from venous blood samples collected in the morning, after overnight fasting.

**Results:** In the first study, no expression of TSHR was detected on the surface of NKT cells, and this result was confirmed at both protein and genetic levels using fluorescence-activated cell sorting (FACS) and RT-PCR. In the second study, a negative, BMI-independent, effect of hyperglycemia on the percentage of CD4-CD8- NKT-like subpopulations was demonstrated. A negative correlation between glucose concentration and the number of CD4-CD8mid cells was also observed, suggesting that even moderate hyperglycemia may lead to alterations in the immunological profile of these cells. In the third study, a positive correlation, independent of total calcium levels, was found between vitamin D concentration and the frequency of CD4-CD8+ NKT-like subpopulations, particularly the CD8high subset, indicating that vitamin D may promote the development and survival of these cells.

**Conclusions:** The presented series of articles broadened the knowledge on factors influencing NKT-like cells and their subpopulations. It was shown that these cells do not express TSHR, which excluded a direct effect of TSH on these cells, particularly in the context of autoimmune thyroid diseases (AITD). It was also demonstrated that even moderate hyperglycemia leads to a significant reduction in the proportion of CD4-CD8- NKT-like subpopulations, which may be associated with increased susceptibility of patients with type 2 diabetes (DM2) to infections and cancers. Moreover, the association between vitamin D levels and the Th1-producing CD4-CD8+ NKT-like subpopulation supports the hypothesis that vitamin D may contribute to regulating the functional activity of these cells. The obtained results emphasize the significance of hormonal factors in modulating immune system functions and may form the basis for developing new diagnostic and therapeutic strategies in autoimmune diseases, cancers, and infectious diseases.