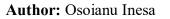


The 10th International Medical Congress For Students And Young Doctors

13. KEY NON-RECEPTOR TYROSINE KINASES IN ADAPTIVE IMMUNITY





Scientific advisor: Simionică Eugeniu, Doctor of Biology, Department of Biochemistry and Clinical Biochemistry, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

Introduction. Non-receptor tyrosine kinases (NRTKs) are cytosolic enzymes, grouped together as a subclass of protein tyrosine kinases (TKs) due to their lack of an extracellular and transmembrane domain, unlike receptor tyrosine kinases (RTKs) – another sub-class of TKs. By means of protein phosphorylation NRTKs activate different signaling pathways, thus regulating a number of cellular functions: growth, proliferation, differentiation, adhesion, migration and apoptosis. Crucial is NRTKs involvement in the adaptive immune system by regulation of B and T cells activation and response.

Aim of study. This study aims to identify NRTKs that are specifically involved in the activation and regulation of adaptive immunity cells.

Methods and materials. A literature review has been performed using PubMed, Elsevier and Hinari databases. A number of 45 scientific articles related to the keywords have been identified, out of which only 37 met the inclusion criteria in the research topic.

Results. Non-receptor tyrosine kinases include 10 families, classified according to their structural and functional differences. Among these, several NRTKs from SYK (ZAP-70, SYK), TEC (ITK, TXK, BTK) and SRC (LCK, FYN, LYN) families have shown to play a critical role in adaptive immunity. In T cells, a signaling cascade is initiated when a T cell receptor (TRS) recognizes a foreign antigen associated with a major histocompatibility complex (MHC). This results in the activation of LCK and FYN, which phosphorylates the ITAM motifs present in the signal-transducing CD3 subunit of the TRC. The recruitment of ZAP-70 then takes place and a series of signaling events are initiated by phosphorylation of two adaptor proteins – LAT and SLP-76. These adaptors create a signaling complex by recruiting several important signaling molecules, including ITK, that activates phospholipase (PLC) γ 1. The subsequent activation of downstream signaling pathways leads to the activation of second messengers and an increase in intracellular Ca2+. Transcriptional modifications are triggered following these events, leading to the production of interleukin-2 (IL-2) and T cell proliferation. ITK and TXK are also involved in T helper cell differentiation, with ITK being expressed in both Th1 and Th2 cells and TXK expression being limited to the Th2 cells only. Unlike T cells, B cells don't require an intermediate MHC for antigen recognition. Thus, after B cell receptor (BCR) binds to the antigen, ITAM domain is exposed and phosphorylated by the LYN kinase. SYK is then recruited and phosphorylates BLNK to form a multi molecular signaling complex with PLC-y2 and BTK. This activates PIP2 and, similar to TCR signaling, leads to second messengers production and intracellular Ca2+ increase, the net result being B-cell proliferation and antibody production.

Conclusion. Non-receptor tyrosine kinases play a central role in B and T cells proliferation and regulation, thus knowledge of NRTKs effects and site of action opens new possibilities for addressing the immune disorders.