

Streszczenie w języku angielskim

The APRIL protein belongs to the TNF superfamily and physiologically leads to faster maturation of granulocytes and plasma cells in the bone marrow and their ejection to the periphery. Unlike many other ligands of the TNF superfamily, it can stimulate the growth of cells of various tumor lines.

Cancer cells do not express the basic receptors of APRIL: TACI and BCMA. On their surface there are heparan sulfate proteoglycans (HSPG), to which APRIL binds. Previous studies have shown that the expression of the APRIL molecule in cancer tissues of various origins and in cells involved in regulating of cancer development.

Head and neck cancers (HNCs), of which more than 90% are squamous cell carcinomas (HNSCCs), are among the most common in the world.

Available data on the effect of APRIL on head and neck squamous cell carcinoma cells are scarce and inconclusive.

The aim of the study was to assess the effect of the recombinant APRIL molecule (rhAPRIL) on the processes of proliferation and apoptosis of cancer cells of selected HNSCC lines and to verify the activity of pro- and anti-apoptotic proteins, as well as the role of the PI3K/p-Akt/survivin pathway in these cells.

The MTT assay was used to assess proliferation, apoptosis was determined by flow cytometry, and protein expression was assessed by Western blot.

In the conducted studies, I demonstrated for the first time the direct effect of rhAPRIL on cells of the FaDu, CAL 27 and SCC-9 lines, expressed in a significant increase in their proliferation and impairment of the apoptosis process, which confirms the pro-cancer activity of this molecule. SCC-9 cells are the most sensitive to the action of rhAPRIL, which is confirmed by the results regarding both proliferation and apoptosis of these cells.

The mechanism of apoptosis inhibition in the tested cell lines in response to rhAPRIL depends to a large extent on changes in the expression of pro- and anti-apoptotic proteins that belong to the Bcl-2 superfamily of the mitochondrial pathway and caspases.

Differences in the expression of the tested pro- and anti-apoptotic proteins in response to the action of rhAPRIL between the tested lines indicate the involvement of other than the tested proteins of the mitochondrial pathway.

The results obtained indicate that the key protein responsible for increased proliferation and impaired apoptosis of the tested HNSCC cell lines in response to rhAPRIL is Survivin.

Analyzing the behavior of proteins of the intracellular signaling pathway, it was shown that among the tested lines, only CAL 27 cells respond to rhAPRIL through the PI3K/Akt/Surwiwin pathway. In the remaining cells, the FaDu and SCC-9 lines, other signaling pathways are probably activated.

The significant effect of APRIL on the process of apoptosis and proliferation of HNSCC tumor cells observed in the conducted studies may be used in the future to improve anticancer therapy in the treatment of HNSCC tumors, based on the regulation of the expression of this molecule.