Abstract of doctoral dissertation, J. Kreczko-Kurzawa MSc., entitled "The role of selected enkephalinase inhibitors in the biology of colorectal cancer. Design and synthesis of anti-cancer compounds based on the structure of sialorphin"

The role of endogenous opioid peptides and enzymes that degrade them in the pathophysiology of tumors has not yet been fully understood.

Numerous studies prove that the components of the opioid system are present not only in healthy cells, for example in the nervous system, but also on the surface of cancerous cells colon, breast, lung, pancreas, thyroid and many others). It has also been found that the processes associated with proliferation, apoptosis, migration and angiogenesis are dependent, among others, on signal peptides and their availability. The effectiveness of peptide mediators is, in turn, regulated by means of proteolysis, which occurs, inter alia, with the participation of cell membrane-associated peptidases such as NEP and APN.

Due to the functionalities of enzymes such as NEP or APN, it can be hypothesized that inhibitors of these enzymes (e.g. sialorphin and other peptides from the opiorfin family) may play a role in carcinogenesis, either through inhibition of enkephalin-degrading proteases or interference with cell pathways signaling via blocking NEP and / or APN functionality not directly related to opioid pathways.

This dissertation presents the results of the first studies on the activity of sialorphin and its modified analogues on the viability and proliferation of colorectal cancer cells, as well as preliminary studies on the effect of sialorphin and its analogs on other cell lines with different NEP expression profiles. In addition, other biological characteristics of sialorphin and selected analogues, such as antimicrobial activity and hemotoxicity, were tested.

This study sheds the new light on structure-activity relationship concerning *in vitro* anti-tumor activity of sialorphin against colon cancer cells. In this work, a number of sialorphin analogues were tested for antitumor activity in the context of the effect on colon cancer cell lines LS180 and SW620, characterized by significant NEP expression.