

## **ROLE OF APELIN AND ITS RECEPTOR IN DEVELOPMENT OF COLON CANCER**

### **DESCRIPTION FOR THE GENERAL PUBLIC**

Colon cancer is an aggressive disease that continues to have a daunting impact on global health. According to the predictions, in next 15 years among people there will be still growing number of colon cancer cases. Despite the fact, that the last years of research gives new ideas and tools for better diagnosis and patient's treatment, in Poland colon cancer is still the second reason of mortality in patients suffering from malignant tumors. It means, that studies about colon cancer biology, which could help to find a new, more effective diagnostic and therapeutic targets are still valid and necessary.

Neoplasia is a long process, consisting of several stages: initiation (first appearance of mutations leading to the creation of the primary cancer cell), promotion (accumulation of genetic changes and uncontrolled cells division), progression (metastasis). Metastasis begins from invasion of tumor cells into closer and more distant tissues and organs. It is believed, that loss of connections between cells is crucial for this. In metastasis, in particular colonization of distant organs, an important role play cells from tumor environment and proteins secreted by them. Therefore, the aims of modern tumor therapy are both tumor cells and normal cells from tumor stroma, which may facilitate the development of tumor cells.

Apelin is a peptide secreted among others by fat cells (adipocytes), which higher level was associated with obesity. Excessive accumulation of body fat in humans is an important risk factor for not only the development of cardiovascular disease, but also is a risk factor of cancer, particularly cancer of the gastrointestinal tract, where adipocytes by the release of a number of factors may stimulate growth of cancer cells. Single reports suggest, that the level of apelin may correlate with the stage and severity of cancer disease. Comparative analysis of the apelin gene expression in normal and tumor tissue showed increased level of apelin in one-third of cancer cases, and even in half of colon cancer cases. Our preliminary studies using colon cancer cells differing in metastatic potential has shown, that these cells have also a different level of apelin gene expression. Therefore, the objective of this project is to determine the role of apelin and its receptor in the progression of colon cancer.

In the first stage of the research I am going to analyze the level of apelin gene and its receptor in the studied cells. Next, the effect of apelin on the growth and invasion of colon cancer cells in different experimental models will be checked. This part of the work will be used to study the relationship between apelin and its receptor, and the invasive abilities of colon cancer cells. In the next stage the role of apelin in modulation of tumor environment will be examined using the co-culture model. This model will help to assess the impact of obesity - adipocytes and factors released by them on the growth and migration of colon cancer cells. Then a series of studies will be performed to explain the observed changes in the cancer cells in response to apelin. In the last step I am going to test the level of apelin and its receptor in the pairs of collected tissue (healthy and tumor) taken from patients with colon cancer. The obtained data will be subjected to statistical comparative analysis.

The proposed project aims to extend the knowledge about the colon cancer biology and the role of tumor microenvironment in its progression. The study will enable a better understanding of the molecular basis of growth and invasion of colon cancer and apelin's functions in these processes. They may also lead to the development of new molecularly targeted diagnostic and therapeutic strategies.