THE ROLE OF RETINOL BINDING PROTEIN 4 (RBP4) IN ANGIOGENESIS AND METASTASIS OF MAMMARY GLAND TUMORS

Retinol binding protein 4 (RBP4) by endothelial damage potentially plays a role in insulin resistance and its consequences at an early stage of development of diabetic angiopathy. RBP4 is involved in the development of cancer too, therefore, the main aim of this reseach was to evaluate the influence of RBP4 on the angiogenesis and metastasis of mouse mammary gland carcinoma.

Conducted studies revealed, that the level of RBP4 in plasma is significantly higher in tumor-bearing mice than in healthy mice. Moreover, the level of RBP4 is correlated with metastatic potential of cancer cells. The concertation of RBP4 in plasma, tumor and liver was higher in mice bearing 4T1 metastatic than in mice bearing 67NR non-metastatic tumors.

The level of RBP4 in breast cancer patients plasma correlated with *severity* of *disease.* Ortotopic injection of 4T1 R4 cells with overexpression of RBP4, caused an increased the numer of metastases in the lungs. Ortotopic injection of 67NR R4 cells (also with RBP4 overexpression) caused lung metastases, whereas wild-type 67NR cells were not observed in the lungs after orthotopic transplantation. In addition, intravenous injection of RBP4 before injection of cancer cells increased the number of tumor cells infiltrating the lungs.

This protein also indirectly affects the angiogenesis process by inducing inflammation and damage of endothelial cells at the early stages of cancer progression. Overexpression of RBP4 in 67NR and 4T1 cell lines, caused the deterioration of the quality of the vessels in the tumor tissue. This correlated with the increase in the number of lung metastases.

The obtained results suggested that RBP4 supports metastasic proces and can be used as a marker of breast cancer. This is important in the case of malignant tumors, where early and proper therapeutic procedures, increase the chance of survival. Nevertheless, further research is necessary in order to thoroughly understand the mechanism of RBP4 functioning or to develop new therapies that effectively block the overexpression of this protein.