Diversification of the microRNA expression profile in plasma and selected tissues in metastatic and non-metastatic breast cancer

The conducted research was aimed at selecting microRNA as a potential marker for the diagnosis of metastatic cancer of the mammary gland. For this purpose, preliminary *in vivo* studies were performed with the use of two murine mammary carcinoma models – the non- metastatic 67NR and the metastatic 4T1 model. Then, the expression level of selected microRNA molecules was determined in cell lysates of murine and human breast cancer cell lines of various molecular subtypes, as well as in plasma and tumor obtained from patients diagnosed with breast cancer. Additionally, the expression level of key markers for the epithelial-mesenchymal transition (EMT) - E-cadherin and N-cadherin was estimated. In order to learn about the function of the selected microRNA molecule - miR-31-5p, its expression was suppressed or increased, then adhesion tests were performed and the expression of selected proteins regulated by miR-31-5p was assessed.

The molecular subtypes of mammary gland cancer differ, for example in the presence of the estrogen α receptor, the progesterone receptor, HER2, wild or mutant form of the p53 protein. The obtained research results indicate that the expression of microRNA, target proteins and selected markers for the EMT process is strictly dependent on the molecular subtype of breast cancer. Interestingly, overexpression of the tested miR-31-5p molecule was observed in HER2 overexpressing cell lines - JIMT-1 and SKBR-3, while lowered expression in other cell lines regardless of the molecular subtype. Overexpression of the studied molecule increases cell adhesion to fibronectin, regardless of the molecular subtype. On the other hand, lowering the expression reduces the adhesion of the tested cell lines to fibronectin. Despite of the initial assumption about protumorigenic function of miR-31-5p, further studies carried on breast cancer cell lines showed that miR-31-5p can play a role as antimetastatic molecule.

The conducted research suggests that miR-31-5p may be a regulator of the EMT process - overexpression of miR-31-5p reduces the expression of the FAK protein and increases adhesion to fibronectin in the TNBC subtype - MDA-MB-468 and in the luminal A subtype. - MCF-7, which may indicate the mentioned antimetastatic properties of this microRNA molecule.