TREATMENT IN BREAST CANCER USING THE CRISPR/CAS9 SYSTEM

Croitoru Dan¹, Corobcean Nadejda², Visnevschi Sergiu¹

¹Department of Human Anatomy and Clinical Anatomy, State University of Medicine and Pharmacy *Nicolae Testemitanu*, Chisinau, Republic of Moldova.

²Department of Oncology, State University of Medicine and Pharmacy *Nicolae Testemitanu*, Chisinau, Republic of Moldova.

Background. Breast cancer is the leading cause of death in the oncological population of female gender and the second most prevalent cause of overall death in the United States of America and the third most prevalent cancer death in Europe. There is a trend for breast cancer in caucasian, hispanic and asian women. Numerous methods of treatment are accepted – chemotherapy, molecular targeted therapy, radiotherapy, immunotherapy, phototherapy and surgical interventions (lumpectomy, mastectomy). The genome editing methods – clustered regularly interspaced short palindromic repeats (CRISPR) technology is developed based on the protection systems found in bacteria, the one which is useful in treating cancer is the Cas9 protein thus defining the CRISPR-Cas9 system. It's main components are crRNA and tancrRNA (sgRNA) with the Cas protein.

Material and methods. We used the PubMed database in order the collect the information. After introducting the key-words "CRISPR-Cas9" and "breast cancer" we revealed up to 571 sources. We have reviewed the first 100 sources and have studied 18 of them. One source was added non-sistematically. Overall we have reviewed 19 sources.

Results. The CRISPR-Cas9 system can be delivered to the target cells via protein, lipid, polymer and inorganic based nanocarriers. Other method of delivery is via the lentiviral/adenoviral vectors. The most efficient ones are the gold nanocarriers (inorganic). The genome editing technology is based on plasmid systems that act via interference and activation thus making them useful for identifying biomarkers and in the diagnosis of breast cancer. The main genes that are targeted by the CRISPR-Cas9 system in breast cancer are BRCA1, BRCA2, MYC, CDK9, UBR5, ZNF319 kinome (HER2, PI3KCA and FGFR), CXCR4+CXCR7 (CXCL) and other tumour supressor genes (p53, PTEN, RB1 and NF1). The genes involved in metabolic pathways are upregulated in a secondary manner because of alterations in canceromatous states. Carcinogenesis, metastasis and resistance to drugs and radiotherapy is reduced after using this treatment method.

Conclusions. CRISPR-Cas9 system is efficient in breast cancer treatment and diagnosis. It has perspectives in order to be used as an adjuvant method in this condition without regard to it's high costs.

Keywords: CRISPR-Cas9, breast cancer, drug resistance, radioresistance.