

miRNA-REGULATED PATHWAYS OF CD8+ T CELLS IN TNBC MOUSE MODEL

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ABSTRACT

Objective: Triple negative breast cancer, which constitutes 20% of all breast cancer is the most aggressive breast cancer subtype. Although breast cancer is known as immune cold, recent studies have revealed that there is an immune response on the basis of subtypes. miRNAs are involved in regulating many biological processes of CD8+ T lymphocytes, which are adaptive immune system cells that effectively destroy tumor cells. Our aim is to examine the regulative roles of miRNAs in CD8+ T lymphocytes during the formation of triple negative breast tumors in mice.

Materials and Methods: 4T1 cells and Balb/c mice were used for the allograft breast cancer model. After 2 weeks, tumor-bearing and control mice were sacrificed, and spleens were harvested for CD8+ T cell isolation. Following RNA isolation, miRNA microarray analysis was performed. Differentially expressed miRNAs between the groups were detected. DIANA-mirPath web tool was used to investigate the target genes of miRNAs and in which pathways these genes are enriched.

Results: Microarray analysis indicated that 41 miRNAs are differentially expressed in CD8+ T cells from tumor-bearing mice compared to the control group. The KEGG analysis results showed that the targets of differentially expressed miRNAs were significantly enriched in immune response-related pathways like ECM-receptor interaction, PI3K-Akt signaling, and tryptophan metabolism pathways.

Conclusion: The pathways in which miRNA-target genes are enriched are associated with T cell metabolism and cell survival. It may be concluded that there are changes in the systemic adaptive immune response during TNBC formation and that miRNAs regulate these changes.

Keywords: Triple Negative Breast Cancer, CD8-Positive T-Lymphocytes, Adaptive Immune Response, microRNA