Alexandria University
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Department of Applied Medical Chemistry

Molecular Study on the Gene Expression of Vitamin D Receptor and MicroRNAs in Egyptian Breast Cancer Female Pateints

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VI- SUMMARY

Breast cancer is the second leading cause of cancer death in women. In USA about 19% of breast cancers are diagnosed in women ages 30-49 years, and 44% occur among women who are age 65 years or older.

The median age at diagnosis in Arab populations, is about 48 years, and about two-third of women with breast cancer are younger than 50 years. In Egypt the incidence rate of breast cancer is 29.9/100,000 population in the age group of 30-34 years.In Alexandria 2016, it accounts for 36 % of all malignancies in females.

The present study was designed to investigate the expression pattern of VDR gene in malignant breast cancer tissues in comparison with the adjacent noncancerous tissues together with the expression pattern of two microRNAs (miR-27b and 125a) as an upstream factors that regulate the stability of VDR mRNA and as a tumor suppressors that may involved in the carcinogenesis. Also, the aromatase expression in malignant and noncancerous breast tissues was assayed. All these parameters were measured in the malignant breast tissue and adjacent apparently apparently normal breast tissue from 50 females of histopathologically proved breast cancer patients.

Total RNA was isolated from malignant breast tissue and adjacent apparently apparently normal breast tissues. Reverse transcription was done by performing a one-step, single-tube reverse transcription reaction to convert all RNA species into cDNA. Gene expression analysis of miR-125a, miR-27b, VDR and aromatase was estimated using RT-PCR.

The results indicated that, the malignant tissues showed significant up-regulation in the expression of VDR compared to the adjacent apparently normal tissues. The malignant tissues of postmenopausal patients have significant higher VDR expression level compared to the premenopausal patients.

The malignant tissues of breast cancer patients showed significantly suppression of miR-125a expression (by about 88%) compared to the adjacent non-cancerous tissues indicating severe down regulation of miR-125a. The malignant tissues of premenopausal patients showed significantly lower expression level of miR-125a compared the malignant tissues of postmenopausal patients.

Regarding the expression of miR-27b in malignant and apparently normal tissues with relative expression in malignant tissues about 1.33 -fold apparently normal value, indicating higher level by about 33% than apparently normal tissues. The premenopausal tumor tissues showed 1.5-fold expression relative to apparently normal tissues which not significantly differ from the postmenopausal tumor which showed about 1.2-fold expression.

The results indicated that the expression of aromatase gene was upregulated in malignant breast tissues compared to adjacent apparently normal tissues especially in premenopausal patients which showed more than 3-fold increase in malignant tissues.

These studied parameters were shown to be affected by the status of different receptors (PR,ER and Her2) in the malignant tissues.

The correlation studies indicated a negative relation between VDR gene expression and miR-125a, miR-27b and aromatase gene expression.

From the data of the present study we can concluded that:

1- The gene expression of VDR is upregulated in the malignant breast tissues compared to adjacent apparently normal tissues

2- VDR gene expression in malignant breast tissues is controlled by the expression of miR-125a and miR-27b

3- The tumor suppressor miR-125a showed severe downregulation in breast malignant tissues

4- VDR gene expression appear to be affected by aromatase gene expression which showed up regulation in malignant breast tissues

5- The crosstalk between VDR and miR-125a, miR27b and aromatase may determine the subset of patients that could be responsive to adjuvant treatment with vitamin D agonist

6- According to the results of VDR expression and other parameters, postmenopausal patients may be more sensitive for vitamin D therapy than premenopausal patients.