PRECIOUS INFORMATION TOWARDS PROGNOSIS, THERAPY AND TUMOR MANAGEMENT

The transformation of normal cells to cancer cells is caused by the abnormal expression of several genes with important cellular functions. The rapid development of molecular sciences in recent years contributed to revealing the identity of many of these genes. Also demonstrated the role of these genes in the mechanism of development, behavior and response of cancer cells to treatment. A modern and accurate way to accessing the activity of these genes is through gene expression and molecular profiling of the tumor.

Determination of gene expression is conducted by the method of quantitative Real Time PCR (Figure 1). The more active is a gene, the more copies of its corresponding mRNA will be present in the isolated mRNAs tank. Conversely, the less active is a gene the fewer the copies of mRNA will be. By using unique primers and/or probes for each gene the number of copies of mRNA for each particular gene analyzed can be determined with great accuracy. By this way, we can be easily identify overactive and underactive genes for a certain tumor compared with the ones of a corresponding normal tissue. Thus, we can outline major mechanisms of tumor development and possible targets for personalized therapy.

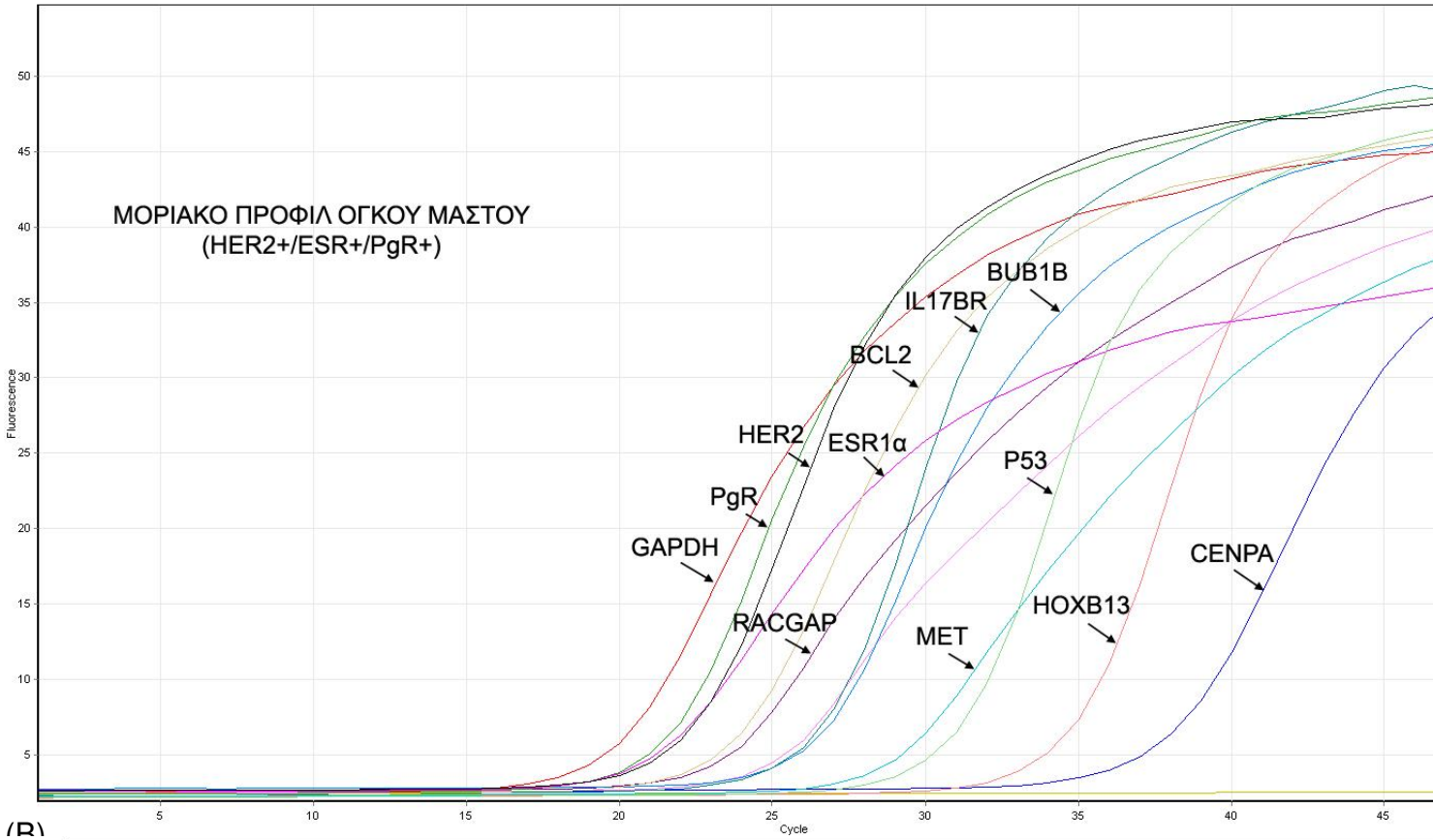
The molecular profile of breast cancer tumor

For the production of a molecular profile of a breast tumor, the expression of certain genes is determined. Such genes are the ones coding for tyrosine kinase receptors (RPTKs), (HER2, EGFR, ERBB3, MET), estrogen receptors (ESR1α, PgR), the chemokine receptor CXCR4 which is associated with the metastatic potential, the transcription factor HOXB13, the interleukin receptor IL17BR, the expression and simultaneously the detection of common mutations in tumor suppressor genes, (p53, PTEN) and the expression of the antiapoptotic genes BCL2 and SURVIVIN. By studying the expression of these genes we know the prognosis that will have the particular mammary tumor and in combination with a mitotic index gene signature (BUB1B, CENPA, NEK2, RACGAP1, RRM2) its risk. Furthermore, the expression of certain genes (ERCC1, BRCA1, RRM2, TYMS, IFIT3, BUB3, BAG1, MAPK14) is monitored to determine the response of cancer cells in common chemotherapeutic drugs (Figure 1).

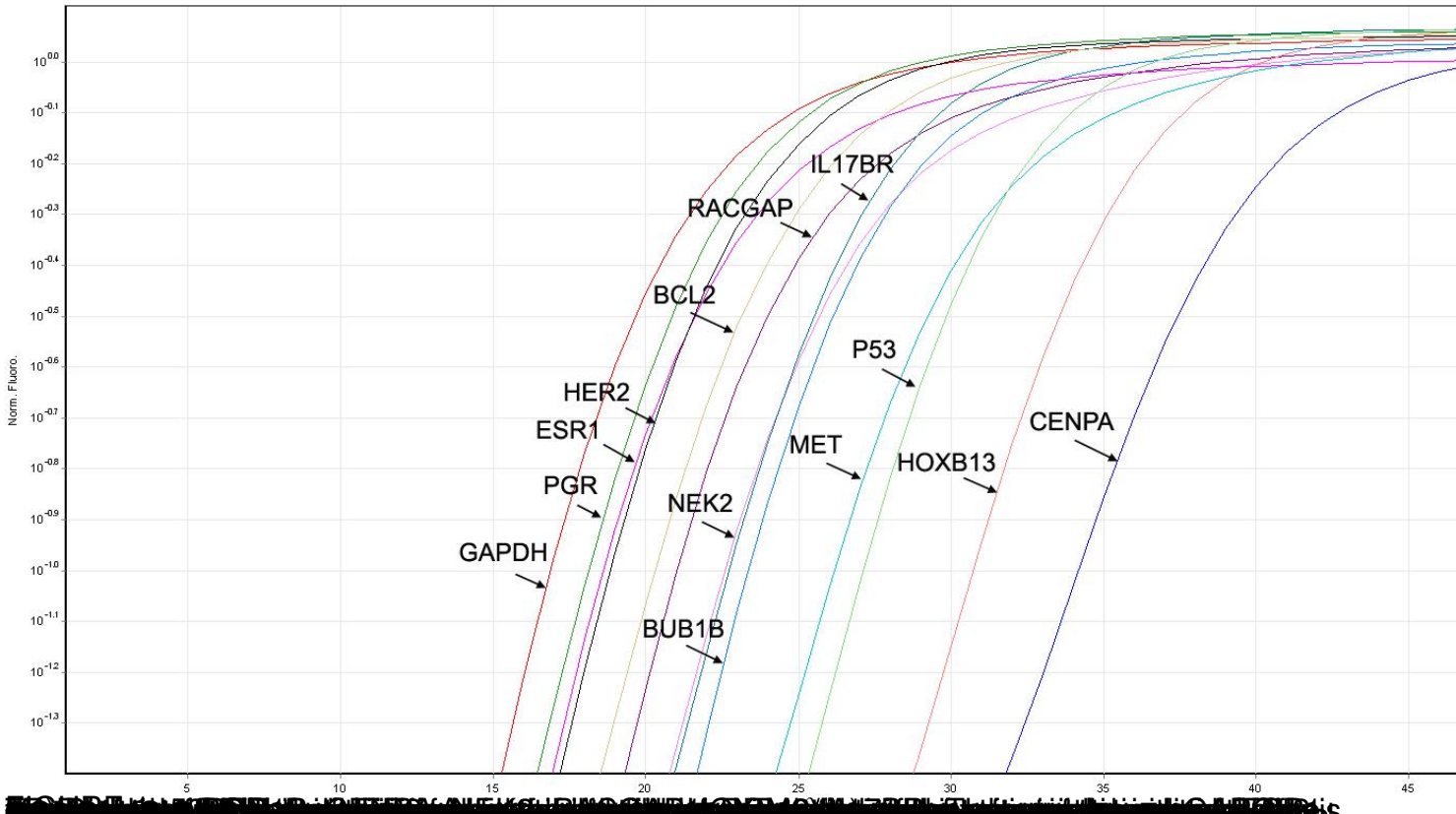
The advantages of gene expression compared to immunohistochemical methods

It is scientifically accepted that gene expression and immunohistochemistry provide comparable results. However, a major advantage of gene expression in relation to the immunohistochemical methods is the small amount of sample required. Even a fine needle biopsy (FNA) can reveal the expression of dozens of genes, which is almost impossible with immunohistochemistry. Furthermore, the expression of the analyzed genes is measured accurately and quantitatively compared to other reporter genes whose expression is not altered in pathological conditions, in contrast to the immunohistochemistry where the occurrence and intensity of a color that indicates the expression of the corresponding protein is monitored. Moreover, by using gene expression analysis, common technical problems such as availability and functionality of certain antibodies used in immunohistochemistry are overcomed.

(A)


ΜΟΡΙΑΚΟ ΠΡΟΦΙΛ ΟΓΚΟΥ ΜΑΣΤΟΥ
(HER2+/ESR+/PgR+)
Fluorescence
Cycle
BUB1B
IL17BR
BCL2
HER2
ESR1α
P53
PgR
GAPDH
CENPA
HOXB13
RACGAP
MET

(B)


Norm. Fluoro.
IL17BR
RACGAP
BCL2
P53
HER2
ESR1
CENPA
MET
HOXB13
PGR
NEK2
GAPDH
BUB1B