

genes included UBE2C, KPNA2, TPX2, FOXM1, STK6, CCNA2, BIRC5, and MYBL2. The trivial names for all of these genes, as well as the nucleotide sequences of these genes, can easily be found at: www.ncbi.nlm.nih.gov.

These two groups, high GGI versus low GGI, represented two subgroups of the study population. A Kaplan–Meier plot was used to present the data, where the plot had two different curves. One curve corresponded to high GGI patients experiencing distant metastasis, while the other curve corresponded to low GGI patients experiencing distant metastasis. The results demonstrated that a low GGI score is prognostic for good outcome, while a high GGI score is prognostic for poor outcome.

An eventual goal of the researchers was to use the 97-gene microarray for guidance in choosing the best treatment for breast cancer patients.

V. USE OF MICRO-RNA EXPRESSION DATA AS A PROGNOSTIC FACTOR FOR BREAST CANCER PATIENTS – THE FOEKENS STUDY

In a study of breast cancer patients, Foekens et al. (22) examined gene expression by tumor biopsies, and attempted to find correlations between gene expression and the endpoint of TDM. All of the genes were in a class called micro-RNA (miRNA). All of the biopsies were from tumors that were ER positive (ER+). A gene array consisting of 249 different miRNA sequences was used, and a comparison of expression versus TDM revealed a specific group of genes, showing a large expression difference in patients with a poor TDM versus in patients with a favorable TDM. This specific group of genes included, *miR-7*, *miR-22*, *miR-34b*, *miR-128a*, *miR-145*, *miR-151*, *miR-193b*, *miR-205*, *miR-210*, *miR-449*, *miR-489*, and *miR-516-3p*. These were the most differentially expressed miRNAs, as determined by comparing biopsy expression data from patients having an early TDM versus patients with a late TDM.

In an exploration of possible associations of these miRNAs with characteristics of the tumors, the researchers found a positive association of *miR-7*, *miR-34b*, and *miR-151* with **tumor size** ($P < 0.05$), and the association of *miR-7*, *miR-210*, *miR-489*, and *miR-516-3p* with **pathological grade** ($P < 0.01$). Further analysis of the 249 genes revealed one group of miRNAs (“cluster 1”) that was associated with good prognosis, that is, a greater value for TDM, and another group of miRNAs (“cluster 3”) that was associated with poor prognosis, that is, a small value for TDM.

To summarize, the study found that specific miRNA sequences were differentially expressed when comparing poor TDM patients with favorable TDM patients. Moreover, the study found that specific miRNA sequences were correlated with tumor size. Also, certain miRNA sequences were associated with pathological grade.

²² Foekens JA, Sieuwerts AM, Smid M, et al. Four miRNAs associated with aggressiveness of lymph node-negative, estrogen receptor-positive human breast cancer. *Proc Natl Acad Sci USA*. 2008;105:13021–13026.