Microarray Study in Cancer : An Example of Mechanistic Analysis on Brain-Specific Metastasis of Breast Cancer Cells

Woong-Yang Park, M.D., Ph.D.

Department of Biochemistry and Molecular Biology, Seoul National University College of Medicine, Seoul, Korea

After the completion of Human Genome Project, we can access to the information on nucleotide sequences of whole human genome. Especially we can have valuable information on the list of approximately 40,000 genes in human genome. Although half of them are still needed to annotate their functions, we can genome-widely screen the alteration of genes in human cancer. To analyze whole genome in their transcription levels, we need high-throughput technology like DNA microarray. It can successfully provide a stable platform technology for the massive screening of genomes rapidly. Microarrays can be used to obtain genome-wide fingerprint on transcriptional changes in various physiological and pathological conditions, leading to the mining novel genes related to tumorigenesis. We can check the multiple molecular markers for diagnosis, prediction or prognosis of human cancers.

During distant metastasis of breast cancer cells, multiple genetic changes are required to survive in a new environment. Brain metastasis is not a frequent event in breast cancer patient, but it can be a good model to study the procedure for distant metastasis and brain stem cells. To establish a animal model for brain metastasis, MDA-MB-435 human breast cancer cells were injected into C57BL/nu immunodeficient mice through left ventricle of heart, and metastatic tumor mass grown in the brain parenchyma was isolated and expanded for molecular analysis. Metastatic tumor cells were then re-introduced into internal carotid artery to get brain-specific metastatic tumor cells. The latent period to have metastatic tumor mass in brain was shortened by repeated injections. To understand the molecular changes in series of metastatic tumor growth, we have examined the whole-genome analysis on the expression profile of these metastatic cells using microarray. We could select differentially expressed genes(DEGs) in highly metastatic tumor cells by F-test (1,182 up- and 834 down-regulated genes). In the list of DEGs, we could find the signature of metastasis-related genes in category of angiogenesis, migration, tumorigenesis and cell cycle. Among these DEGs, group of genes related to Notch signaling was significantly increased in metastatic tumor cells. In these results, we suggest that brain-specific metastasis model could enrich the population of metastatic breast cancer cells, in which the activation of Notch signaling might play a crucial role.