INTRODUCTION

During the past 25 years, technical advances in nucleic acid analysis and methods have allowed scientists to identify several qualitative and quantitative changes in DNA and RNA sequences, and ultimately, in proteins that can result in the development of cancer. Microarray technology yields far more data, much more rapidly than previously known methods.

Microarrays are hundreds, thousands, or even tens of thousands of miniature assays for biomolecules such as DNA, RNA, and proteins. This review considers the main types of DNA microarrays, the kinds of information they provide, how that information is changing the way we think about cancer and carcinogenesis, and the expanding role of this technology in clinical oncology. Protein microarrays and tissue microarrays are not discussed in detail here, but the interested reader is referred to recent reviews.1-6

DNA MICROARRAYS AS DIAGNOSTIC AND PROGNOSTIC TOOLS

The successful clinical management of human malignancies requires an ever-evolving arsenal of both diagnostic and prognostic methods, and microarray analysis may be able to serve as a new tool that provides useful information for both. Currently, histopathologic evaluation of tumor type and grade, and pathologic and clinical assessment of a cancer’s stage are the mainstays for guiding therapeutic interventions and predicting outcomes. These data are usually supplemented with information from the patient’s history, the physical exam, imaging tests, and clinical laboratory assays of tumor markers.

However, even the combined use of all available clinical and laboratory information remains suboptimal for diagnosis, for predicting prognosis, and for predicting patient response to specific therapies. Tumors with identical histopathologies may progress differently, may respond differently to therapy, and may be associated with widely divergent clinical outcomes, suggesting that additional factors may be directing disease outcomes. DNA microarray technology may be a more comprehensive determinant for guiding therapeutic interventions in the future.

Recent efforts to define factors or variables that guide tumor progression have focused on the molecular genetic definition of cancer. Early efforts focused at the DNA level endeavored to “allelotype” human tumors and attempted to identify DNA-base sequence deletions, insertions, or mutations associated with disease progression and clinical outcomes. For example, variation in...
nucleotides in specific positions of a sequence may or may not alter the functional activity of the protein encoded by that gene. Some of these variations may involve single nucleotides, and are called single nucleotide polymorphisms—abbreviated SNPs and pronounced “snips.” Some SNPs result in protein variants, while others do not directly alter a protein, but are linked to, and therefore act as, markers for another sequence change that is functionally significant. The discovery and cataloguing of these single nucleotide variations, has been enormously facilitated by the human genome project. Use of DNA microarrays is now revealing associations of specific SNPs with cancer risk, development, and progression at a substantially accelerated pace.

Other efforts are focused at the transcriptional or RNA level. These attempt to “profile” the gene transcription pattern of normal and malignant tissues using cDNA microarrays—a new high-throughput technology.

## TYPES OF DNA MICROARRAYS

There are two basic varieties of DNA microarrays: spotted or cDNA microarrays and oligonucleotide microarrays. The first, cDNA or spotted arrays, are created by the deposition of concentrated solutions of double-stranded DNA on a grid. A variety of automated devices are available that can precisely control the amount and position of the DNA spots. The DNA sequences, usually somewhat longer than 100 nucleotide-base pairs, are typically polymerase chain reaction (PCR) products from the amplification of recombinant cDNA library clones.7,8

Oligonucleotides are shorter sequences—usually 16 to 20 base pairs. Sometimes the oligonucleotides are deposited onto glass slides by spotting or by using miniature devices similar to ink jet printers. Increasingly, oligonucleotide arrays are created through a photolithographic process similar to the way computer chips are made.9,10 The oligonucleotide density that can be achieved on such arrays is quite high, with recent arrays representing 12,000 sequences at 16 to 20 oligomers per sequence for a total of 192,000 to 240,000 oligonucleotides per chip.

Both spotted and oligonucleotide arrays can be used to study gene expression. Messenger RNA is extracted first because it actually measures gene expression. But the RNA sample is reverse transcribed back to complementary DNA (cDNA), which is less susceptible to degradation and can be amplified by PCR, an important strategy used to analyze very small samples.

Analysis of DNA sequences generally uses oligonucleotide microarrays. Some of these arrays contain oligonucleotides designed to recognize SNPs of many genes. These are sometimes referred to as “snip chips.” Other oligonucleotide microarrays are designed to detect all or most of the possible sequence variations in a single gene. These are sometimes called sequencing or resequencing microarrays. The latter term seems more technically accurate, since the microarrays can be designed only after the gene’s sequence has already been determined by conventional methods.

Before their analysis using either oligonucleotide or spotted arrays, samples of genomic DNA or of cDNA are labeled with fluorescent markers. Fluorophores such as Cy3 or Cy5 emit light of different wavelengths that are usually visualized as red (Cy5) or green (Cy3) after excitation with the appropriate lasers. The intensity of the resulting fluorescent signal is quantified by the laser scanning instrument and is proportional to the quantity of DNA deposited on the slide. In this way, cDNA microarrays can be used to determine whether and how much specific genes are transcribed in any given tissue or source of

---

Volume 52 • Number 1 • January/February 2002

51

CA Cancer J Clin 2002;52:50-59
cellular material (Figure 1).

Two cDNA samples, each labeled with a different color marker, can be simultaneously applied to the same microarray. By comparing the intensity of each color, it is possible to compare the relative degree of transcriptional activity of thousands of specific genes in, for example, benign tissue and malignant tumors, different types of malignancies, or malignancies of the same type from patients known to have had different clinical outcomes (Figure 2).

Several algorithms have evolved for handling and statistically analyzing the large quantities of data generated by single and multiple microarray experiments. Recent efforts that encourage the dissemination and sharing of large microarray-acquired datasets may speed the development of analytic tools for data

---

**FIGURE 1**

CDA Microarray Schema: Templates for genes of interest are obtained and amplified by PCR. Following purification and quality control, cDNAs are printed onto coated glass microscope slides using a computer-controlled, high-speed robot. Total RNA from both the test and reference sample are fluorescently labeled using a single round of reverse transcription. The fluorescent targets are pooled and allowed to hybridize under stringent conditions to the clones on the array. Laser excitation of the incorporated targets yields an emission with a characteristic spectra, which is measured using a laser scanning instrument. Information about the clones, including gene name, clone identifier, intensity values, intensity ratios, normalization constant, and confidence intervals, is attached to each target. Data from a single hybridization experiment is viewed as a normalized ratio (that is, Cy5/Cy3) in which significant deviations from 1 (no change) are indicative of increased (> 1) or decreased (< 1) levels of gene expression relative to the reference sample. In addition, data from multiple experiments can be examined using any number of data mining tools. Reprinted with permission from: Duggan DJ, Bittner M, Chen Y, Meltzer P, Trent JM. Expression profiling using cDNA microarray. Nature Genetics 1999;21:10-14.
Panel A is an image of a cDNA microarray after the cohybridization of fluorescently-labeled probes. Individual genes are laid out in a grid pattern with a corresponding "column" and "row" address location. Each probe was made from reverse-transcribed RNA from different tissues. Probe 1, from Tissue 1, was labeled with the Cy5 fluorophore; Probe 2, from Tissue 2, was labeled with Cy3. Spots that appear predominantly red represent genes expressed at higher levels in Tissue 1 (e.g., RSN); spots that appear predominantly green represent genes expressed at higher levels in Tissue 2 (e.g., PTB). Other spots appear yellow, demonstrating equal expression of the corresponding genes in Tissues 1 and 2.

Panel B is a table listing quantitative differences in gene expression between Tissues 1 and 2 revealed by the cDNA microarray experiment. The column and row addresses of 13 differentially expressed genes are provided, as are the gene names (represented by their official Human Genome Organization gene symbols) and GenBank accession numbers. The actual laser scanner “readings” of gene expression intensity levels are provided for Probe 1 (for Tissue 1) and Probe 2 (for Tissue 2). The Log Ratio refers to the base 2 exponent of the Cy5/Cy3 (e.g., Tissue 1/Tissue 2) ratio. Log Ratios > 1 correspond to a 2x or more increase, whereas Log Ratios < -1 correspond to a 2x or more decrease, in gene expression in Tissue 1 compared with Tissue 2. This is shown in the last column of the table, which lists the actual fold difference in expression for each of the 13 genes for Tissue 1 compared with Tissue 2. For example, expression of the RSN gene is 2.070 fold more abundant in Tissue 1 compared with Tissue 2, whereas expression of the PTB gene is 2.481 fold less abundant in Tissue 1 compared with Tissue 2.
adenomas, and colonic tumors. These profiles permitted the investigators to classify each of the 22 samples studied as normal, adenomatous, or malignant with no discordance between diagnoses based on gene expression and histopathology.

The expression profiles obtained for adenomas were consistent with their potential role as precursor lesions to colonic adenocarcinomas and may help define early genetic events in colon carcinogenesis. Another recent study demonstrated that cDNA microarrays can successfully distinguish adenocarcinomas arising from different tissues, e.g., colon, lung, and ovary. In this study, the analysis of a comprehensive gene expression profile of 57 lung, 51 colon, and 46 ovarian primary adenocarcinomas using high-density oligonucleotide arrays was in agreement with histopathologic assessment of primary sites of 152 of the 154 cases. Interestingly, review of the two discordant cases found that one case, initially diagnosed as a primary ovarian adenocarcinoma, had histology and immunohistochemistry most consistent with a metastasis from a colorectal cancer, and that the other discordant case, a poorly differentiated cancer initially diagnosed as adenocarcinoma, was probably a sarcoma. Analysis identified three subsets, of 20 genes each, that were specifically and differentially expressed for each tumor type. As additional studies confirm and expand upon these findings, cDNA microarrays may find utility in clinical management of patients with metastatic cancer of unknown primary.

**Identifying Disease Subsets**

Gene expression profiles generated by microarrays can be used to identify clinically relevant subsets among patients with histologically indistinguishable tumors.

**Leukemia**

One of the earliest large-scale, gene expression profiling efforts aimed at identifying disease subsets used cDNA microarrays to distinguish acute myelogenous leukemias (AML) from acute lymphocytic leukemias (ALL). Golub and colleagues profiled 38 bone marrow samples containing acute leukemia (27 ALL, 11 AML) for the expression of 6,817 genes using oligonucleotide arrays.

This study identified approximately 1,100 informative genes that were more highly correlated with the AML-ALL class distinction than would be expected by chance. The expression pattern of a smaller subgroup of 50 known highly informative genes was then used to categorize 34 additional acute leukemia samples from bone marrow or peripheral blood.

Twenty-nine of 34 acute leukemias were correctly categorized based on the expression profiling, demonstrating the potential of this approach for tumor-type classification. Moreover, these methods correctly identified ALL subtypes as originating from either B-cell or T-cell lineages.

**Lymphoma**

Alizadeh et al. also used gene expression profiling to identify subclasses of diffuse large B-cell lymphomas (DLBCL), a clinically heterogeneous disease. RNA from 96 lymph nodes with normal histology, DLBCL, follicular lymphoma (FL), or chronic lymphocytic leukemia (CLL) was profiled using a lymphocyte-specific 17,856 gene array. These studies largely segregated normal, DLBCL, FL, and CLL samples from each other based on their gene expression profiles.

Furthermore, analysis of the gene expression profiles revealed two subtypes within DLBCL cases. The two subtypes had gene expression...
profiles resembling either germinal center B cells or activated peripheral blood B cells, suggesting that lymphomas currently diagnosed as DLBCL may actually represent two diseases.

Moreover, the Kaplan-Meier analysis showed that patients with the two DLBCL subtypes had statistically significant differences in overall survival. Five-year survival rates for patients with the germinal center B cell and activated peripheral blood B-cell gene expression patterns, were 76 percent and 16 percent respectively.

These studies demonstrate the power of cDNA microarray technology to discern otherwise unrecognized disease subtypes of distinct origin and clinical outcomes.

**Breast Cancer**

Several recent studies have focused on expression profiling of human breast tumors. Perou et al. profiled 65 surgical specimens from 42 individuals for the expression levels of greater than 8,000 transcripts. Twenty cases were sampled twice, once before and once after a 16-week course of doxorubicin chemotherapy. Analysis of the resulting data demonstrated that chemotherapy did not markedly alter the gene expression patterns of the treated tumors, and that tumors from different individuals exhibited a wide variation in gene expression patterns.

The RNA profiles for 496 genes demonstrating the widest variation in expression were used to divide the clinical specimens into two groups comprising largely ER-positive or ER-negative tumors. A subsequent RNA profiling study by Sorlie et al. succeeded in dividing breast cancers into several prognostically significant categories based on expression profiles, with ER-positive breast cancers subdivided into two groups with significantly different survival rates.

Confirming earlier studies, Sorlie et al. also showed that tumors expressing high-transcript levels of the ErbB2/HER2/neu oncogene segregated into a distinct group that experienced poor long-term survival.

West et al. used Bayesian-based analyses to identify 100 genes whose expression levels best discriminated between ER-positive and ER-negative breast tumors. Many of the 100 genes are either transcriptionally induced by estrogen or encoded proteins that interact with estrogen or are involved in estrogen action. To a lesser extent, the expression profile of the primary tumor for this group of 100 genes correctly predicted axillary lymph-node status, as well.

Finally, a study by Hedenfalk et al. demonstrated distinct RNA expression profiles for sporadic, BRCA1 mutation positive and BRCA2 mutation positive breast tumors. In particular, the RNA expression profiles for the BRCA1 mutation positive tumors showed the coordinated transcriptional upregulation of stress-response genes. Taken together, these studies suggest that RNA profiling can distinguish breast cancer subtypes with biological relevance to hormonal status, cell type, and patient outcomes.

**Prostate Cancer**

Several studies have focused on the use of cDNA microarrays to profile gene expression in prostate lesions. Luo et al. reported that RNA expression profiling easily distinguished prostate cancer from benign prostatic hyperplasia (BPH), even though only three percent of the 6,112 genes examined were differentially expressed by a factor of 1.7x or more between the two lesions.

Dhanasekaran et al. were able to distinguish among normal benign prostate tissue, BPH, localized prostate cancer, and metastatic prostate cancer based on RNA expression profiles. The PIM1 gene was overexpressed at the RNA level in approximately half of all prostate cancers.
Examination of PIM1 protein expression in a large number of specimens clearly demonstrated a significant and positive association between high PIM1 expression and enhanced patient survival, suggesting that the PIM1 protein might have value as a prognostic biomarker. In a multivariate Cox model that also included the Gleason score and preoperative PSA level, patients with decreased PIM1 protein expression were 4.5 times more likely to have a PSA relapse than were patients whose tumors had higher PIM1 expression.23 A study by Magee et al. identified a small number of genes that distinguished localized prostate cancer from metastatic prostate cancers.24 Though using different “platforms” (spotted versus oligonucleotide arrays) and different groups of clinical specimens, all three prostate cancer RNA profiling studies identified significant overexpression of the hepsin gene in malignant prostate tissues, though hepsin overexpression was not associated with clinical outcomes.22-24

Renal Cell Carcinoma

A study profiling clear cell type of renal cell carcinomas (ccRCC) distinguished two disease subsets that correlated with cause-specific patient survival at five years. RNA profiling of a small subset of genes successfully “predicted” cause-specific patient survival at five years for 95 percent of ccRCC, suggesting that some of these gene products contributed biologically to differential patient survival rates and may serve as prognostic markers.25

Identifying Therapeutic Targets

A major aim of the studies that profile RNA expression patterns of human tumors is to identify gene products that may serve as useful biomarkers for cancer diagnosis or prognosis or provide new therapeutic targets.

Many of the preceding studies defined genes differentially expressed in particular tumor types or subtypes that may prove useful as biomarkers or therapeutic targets. Other studies have utilized in vitro model systems to further explore the relationship between tumor genotype and phenotype.

One example is the development and RNA expression profiling of a p53-resistant subline of ECV-304 bladder carcinoma cells. The RNA expression patterns of the p53-resistant and parent cell lines differed for 480 genes, including several that are transcriptionally regulated by the p53 gene product and may participate in the p53-mediated apoptosis of tumor cells.26 The identification of potential downstream effectors of p53-mediated apoptosis may facilitate the development of therapeutics that mimic the activities of these effectors and compel tumor cells to undergo death by apoptosis even in the absence of wild-type p53.

Another study demonstrated that the treatment with dexamethasone of two T-lymphocytic leukemia cell lines (Jurkat and CEM-C7) resulted in the differential expression of 98 genes out of 5,600 genes represented on the array. The average degree of transcriptional upregulation was 4.9-fold for a Jurkat expressing stably-transfected wild type glucocorticoid receptor compared with 2.1-fold for a subline expressing a mutant receptor, demonstrating the effects of glucocorticoid-receptor integrity on dexamethasone response.27 This study demonstrates that modulation of the tumor response to therapeutics due to hormone receptor status may be due to the transcriptional activation or inactivation of many genes. The use of cDNA allowed the identification of specific, differentially transcribed genes whose protein...
products may provide additional or alternative therapeutic targets.

Finally a more general strategy recently reported by Diehn et al. developed a centrifugation-based methodology to separate nuclear- and cytosolic-mRNA transcripts encoding membrane-associated or secreted versus cytoplasmic proteins, respectively. These mRNA pools were then reverse transcribed, PCR amplified, sequenced, and spotted onto glass microarrays. The use of these arrays to profile multiple tissue and tumor types may facilitate the identification of new biomarkers in the form of novel secreted proteins that may be detectable in serum or other body fluids. They may also facilitate the identification of new therapeutic targets in the form of membrane-bound tumor antigens that may help direct or target chemotherapeutic agents to particular tumor tissues.

MICROARRAY ANALYSIS OF GENOMIC DNA

Although analysis of gene expression patterns is the most common application of microarray technology, oligonucleotide microarrays have the potential to detect sequence changes in genomic DNA. Studies have compared microarrays and conventional sequencing methods for several cancer-associated genes.

In one of the earliest studies of oligonucleotide microarray sequencing, Hacia and colleagues compared microarrays and conventional sequencing methods for detecting mutations in exon 11 of the BRCA1 gene. Oligonucleotide microarray identified 14 of the 15 mutations found by conventional methods, without any false-positives, among 20 normal samples.

Hacia and colleagues have also applied a similar approach to the ATM gene. Homozygous and heterozygous ATM mutations increase the risk of developing cancer, especially breast cancer. Oligonucleotide microarrays designed to detect all possible mutations of the entire coding sequence were successful in doing so for 17 of 18 heterozygous and eight of eight homozygous mutations.

Wen-Hsiang and colleagues compared microarrays and conventional gel-based methods for identification of p53 gene mutations in ovarian cancer specimens. The conventional strategy, sequencing portions of the gene identified by single-strand conformational polymorphism, was less accurate than the microarray-based method as evaluated by repeat manual or automated sequencing of the full gene.

CONCLUSIONS AND FUTURE MICROARRAY DIRECTIONS

The potential for microarray analysis to assume a significant role in cancer diagnosis and treatment selection is excellent. The importance of microarrays to future progress in oncology and other fields of medicine is supported by the recent appearance of review articles in several clinical journals. Although the technology is
still evolving and its uses are still being explored, the promise demonstrated thus far from research findings on microarrays’ ability to predict prognosis of some diseases is astounding. This brief review serves to illustrate some of this promise. Though they are still preliminary, microarray-based studies have already identified many genes whose protein products might serve as effective biomarkers for cancer diagnoses, prognosis, and individualized treatment selection. These studies have also identified genes whose protein products may provide therapeutic targets for the progressive development of novel, more effective, and less toxic chemotherapeutic agents.

The gene expression profiles obtained by cDNA microarrays may help ascertain the key genetic events underlying tumor initiation, promotion, and progression. This type of genetic information may provide the foundation for the development of either universal or tumor-specific chemopreventive agents. In any event, illumination of DNA-transcriptional events that are perturbed during tumorigenesis as uncovered by microarray analysis will unquestionably pave the way toward more protein-based research efforts to reveal the myriad interplay of protein functions and protein–protein interactions that ultimately contribute to human tumor development.

REFERENCES

1. Huang JX, Mehrens D, Wiese R, et al. High-throughput genomic and proteomic analysis using microarray technology. Clin Chem 2001;47:1912-1916.
2. Banks RE, Dunn MJ, Hochstrasser DF, et al. Proteomics: New perspectives, new biomedical opportunities. Lancet 2000;356:1749-1756.
3. Bischel VE, Liotta LA, Petricoin EE III. Cancer proteomics: From biomarker discovery to signal pathway profiling. Cancer J 2001;7:69-78.
4. Srinvas PR, Srivastava S, Hanash S, et al. Proteomics in early detection of cancer. Clin Chem 2001;47:1901-1911.
5. Hoos A, Cordon-Cardo C. Tissue microarray profiling of cancer specimens and cell lines: Opportunities and limitations. Lab Invest 2001;81:1331-1338.
6. Nocito A, Kononen J, Kallioniemi OP, et al. Tissue microarrays (TMAs) for high-throughput molecular pathology research. Int J Cancer 2001;94:1-5.
7. Pease AC, Solas D, Sullivan EJ, et al. Light-generated oligonucleotide arrays for rapid DNA sequence analysis. Proc Natl Acad Sci U S A 1994;91:5022-5026.
8. Chee M, Yang R, Hubbell E, et al. Accessing genetic information with high-density DNA arrays. Science 1996;274:610-614.
9. Schena M, Shalon D, Davis RW, Brown PO. Quantitative Monitoring of Gene Expression Patterns with a Complementary DNA Microarray. Science 1995;270:467-470.
10. Schena M, Shalon D, Heller R, et al. Parallel human genome analysis: Microarray-based expression monitoring of 1000 genes. Proc Natl Acad Sci U S A 1996;93:10614-10619.
11. Eisen MB, Spellman PT, Brown PO, Botstein D. Cluster analysis and display of genome-wide expression patterns. Proc Natl Acad Sci U S A 1998;95:14863-14868.
12. Lu J, Liu Z, Xiong M, et al. Gene expression profile changes in initiation and progression of squamous cell carcinoma of esophagus. Int J Cancer 2001;91:288-294.
13. Geschwind DH. Sharing gene expression data: An array of options. Nat Rev Neurosci 2001;2:435-438.
14. Notterman DA, Alon A, Sierk AJ, Levine, AJ. Transcriptional gene expression profiles of colorectal adenoma, adenocarcinoma, and normal tissue examined by oligonucleotide arrays. Cancer Res 2001;61:3124-3130.
15. Giordano TJ, Shedden KA, Schwartz DR, et al. Organ-Specific Molecular Classification of Primary Lung, Colon, and Ovarian Adenocarcinomas Using Gene Expression Profiles. Am J Pathol 2001;159:1231-1238.
16. Golub TR, Slonim DK, Tamayo P, et al. Molecular Classification of Cancer: Class Discovery and Class Prediction by Gene Expression Monitoring. Science 1999;286: 531-537.
17. Alizadeh AA, Eisen MB, Davis RE, et al. Distinct types of diffuse large B-cell lymphoma identified by gene expression profiling. Nature 2000;403:503-511.
18. Perou CM, Sorlie T, Eisen MB, et al. Molecular portraits of human breast tumours. Nature 2000;406:747-752.
19. Sorlie T, Perou CM, Tibshirani R, et al. Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. Proc Natl Acad Sci U S A 2001;98:10869-10874.
20. West M, Blanchette C, Dressman H, et al. Predicting the clinical status of human breast cancer by using gene expression profiles. Proc Natl Acad Sci U S A 2001;98:11462-11467.
21. Hedenfalk I, Duggan D, Chen YD, et al. Gene-expression profiles in hereditary breast cancer. N Engl J Med 2001;344:539-548.
22. Luo J, Duggan DJ, Chen Y, et al. Human prostate cancer and benign prostatic hyperplasia: Molecular dissection by gene expression profiling. Cancer Res 2001;61:4683-4688.
23. Dhanakumar SM, Barrett TR, Ghosh D, et al. Delineation of prognostic biomarkers in prostate cancer. Nature 2001;412:822-826.
24. Magee JA, Araki T, Patil S, et al. Expression profiling reveals hepsin overexpression in prostate cancer. Cancer Res 2001;61:5692-5696.
25. Takahashi M, Rhodes DR, Furge KA, et al. Gene expression profiling of clear cell renal cell carcinoma: Gene identification and prognostic classification. Proc Natl Acad Sci U S A 2001;98:9754-9759.
26. Maxwell SA, Davis GE. Differential gene expression in p53-mediated apoptosis-resistant vs. apoptosis-sensitive tumor cell lines. Proc Natl Acad Sci U S A 2000;97:13009-13014.
27. Obexer P, Certa U, Kofler R, Helmberg A. Expression profiling of glucocorticoid-treated T-ALL cell lines: Rapid repression of multiple genes involved in RNA-, protein-, and nucleotide synthesis. Oncogene 2001;20:4324-4336.
28. Diehn M, Eisen MB, Botstein D, Brown PO. Large-scale identification of secreted and membrane-associated gene products using DNA microarrays. Nat Genet 2000;25:58-62.
29. Chicurel M. Faster, better, cheaper genotyping. Nature 2001;412:580-582.
30. Hacia JG, Brody LC, Chee MS, et al. Detection of heterozygous mutations in BRCA1 using high density oligonucleotide arrays and two-colour fluorescence analysis. Nature Genet 1996;14:441-447.
31. Hacia JG, Sun B, Hunt N, et al. Strategies for mutational analysis of the large multiexon ATM gene using high-density oligonucleotide arrays. Genome Res 1998;8:1245-1258.
32. Wen-Hsiang W, Bernstein L, Lescallett J, et al. Comparison of TP53 mutations identified by oligonucleotide microarrays and conventional DNA sequence analysis. Cancer Res 2000;60:2716-2722.
33. Atman TJ. DNA microarrays in medical practice. BMJ 2001;323:611-615.
34. Rew DA. DNA microarray technology in cancer research. Eur J Surg Oncol 2001;27:504-508.
35. Cooper CS. Applications of microarray technology in breast cancer research. Breast Cancer Res 2001;3:158-175.
36. Bubendorf L. High-throughput microarray technologies: From genomics to clinics. Eur Urol 2001;40:231-238.