An Integrated Database of Chemosensitivity to 55 Anticancer Drugs and Gene Expression Profiles of 39 Human Cancer Cell Lines

Shingo Dan, Tatsuhiko Tsunoda, Osamu Kitahara, Rempei Yanagawa, Hitoshi Zembutsu, Toyomasu Katagiri, Kanami Yamaizaki, Yusuke Nakamura, and Takao Yamori

Division of Molecular Pharmacology, Cancer Chemotherapy Center, Japanese Foundation for Cancer Research, Toshima-ku, Tokyo 170-8455 [S. D., K. T., Y. T.]; Laboratory of Molecular Medicine, Human Genome Center, Institute of Medical Science, The University of Tokyo, Minato-ku, Tokyo 108-8639 [O. K., R. Y., H. Z., T. K., Y. N.]; and SNP Research Center, RIKEN (Institute of Physical and Chemical Research), Minato-ku, Tokyo 108-8639 [T. T.]; Japan

ABSTRACT
To explore genes that determine the sensitivity of cancer cells to anticancer drugs, we investigated using cDNA microarrays the expression of 9216 genes in 39 human cancer cell lines pharmacologically characterized on treatment with various anticancer drugs. A bioinformatical approach was then exploited to identify genes related to anticancer drug sensitivity. An integrated database of gene expression and drug sensitivity profiles was constructed and used to identify genes with expression patterns that showed significant correlation to patterns of drug responsiveness. As a result, sets of genes were extracted for each of the 55 anticancer drugs examined. Whereas some genes commonly correlated with various classes of anticancer drugs, other genes correlated only with specific drugs with similar mechanisms of action. This latter group of genes may reflect the efficacy of each class of drugs. Therefore, the integrated database approach of gene expression and chemosensitivity profiles may be useful in the development of systems to predict drug efficacies of cancer cells by examining the expression levels of particular genes.

INTRODUCTION
Despite enormous efforts spent in the development of cancer chemotherapy, often these therapies are effective only in a relatively small proportion of cancer patients. Whereas it has been long recognized that the effectiveness of anticancer drugs can vary significantly among individuals, the same protocols are often applied without consideration of the different cancer cell characteristics of each patient. Because at present, there is no way to predict the effectiveness of a cancer chemotherapy for each case, cancer patients are still treated with the same protocols despite the possibility that the treatment may not be appropriate.

Two major factors need to be considered when regarding the efficacy of particular anticancer drugs: (a) local blood or tissue drug concentrations can be influenced by the activities of metabolic enzymes, which may activate or inactivate the drug, and actions of drug transporters; and (b) differences in individual drug efficacies may also reflect the intrinsic susceptibility of cancer cells to those anticancer drugs. In the latter case, a number of genes has been reported to influence chemosensitivity, e.g., cancer cells expressing high levels of P-glycoprotein encoded by the ABCB1 (formerly MDR-1) gene are often resistant to a large subset of anticancer drugs, including vincristine, etoposide, and paclitaxel (taxol; Ref. 1). However, it has become obvious that the susceptibility of cancer cells to particular anticancer drugs cannot be predicted by a single factor but is determined by many factors that influence overall sensitivity. Therefore, to establish an appropriate protocol for the prediction of chemosensitivity, we need to accumulate information on the sets of genes that pharmacologically characterize cancer cells on treatment with particular anticancer drugs.

Taking advantage of a panel of 39 well-characterized human cancer cell lines (2) and a cDNA microarray system consisting of 9216 genes (3), we attempted to reveal genes associated with cancer cell chemosensitivity. Here, we report the construction of an integrated database of gene expression profiles and drug sensitivity patterns for 39 human cancer cell lines and the identification of gene sets that are likely to be involved in chemosensitivity.

MATERIALS AND METHODS

Cell Lines and Cell Culture. The human cancer cell line panel has been described previously (2) and consists of the following 39 human cancer cell lines: lung cancer, NCI-H23, NCI-H226, NCI-H522, NCI-H460, A549, DMS273, and DMS114; colorectal cancer, HCC-2998, KM-12, HT-29, HCT-15, and HCT-116; gastric cancer, MKN-1, MKN-7, MKN-28, MKN-45, MKN-74, and S-4; ovarian cancer, OVCAR-3, OVCAR-4, OVCAR-5, OVCAR-8, and SK-OV-3; breast cancer, BSY-1, HBC-4, HBC-5, MDA-MB-231, and MCF-7; renal cancer, RXF-631L and ACHN; melanoma, LOXIMVI; glioma, U251, SF-295, SF-539, SF-268, SNB-75, and SNB-78; and prostate cancer, DU-145 and PC-3. All cell lines were cultured in RPMI 1640 supplemented with 5% fetal bovine serum, penicillin (100 units/ml), and streptomycin (100 mg/ml) at 37°C in humidified air containing 5% CO2. The cell line panel has been used in anticancer drug screening programs at the Japanese Foundation for Cancer Research (2) and for modeling systems at the Developmental Therapeutics Program of the NCI (4) and has been examined for susceptibility to a number of chemical compounds, including current anticancer drugs.

Growth Inhibition Assay and Data Processing. Growth inhibition was assessed as changes in total cellular protein after 48 h of drug treatment using a sulforhodamine B assay. The GI50 was calculated as described previously (2, 4).

Identification of Gene Expression Profiles by cDNA Microarrays. Cell lines grown as monolayers to log phase were washed twice with PBS, and total RNA was extracted with TRIzol reagent (Life Technologies, Inc.). After treatment with DNase I (Boehringer Mannheim) to remove contaminating genomic DNA, poly(A)+ RNA was extracted using an mRNA Purification Kit (Amersham Pharmacia Biotech). Probe cDNA-labeling reactions for each sample were performed as described previously (5), except that an oligodeoxynucleotide primer was used instead of random hexamers. Each sample was reverse transcribed in the presence of Cy5-labeled dCTP. A mixture of mRNA from all 39 cell lines was prepared as the control probe. The mRNA mixture was amplified by T7-based amplification and reverse transcribed in the presence of Cy3-labeled dCTP, as described previously (5–7). Sample and control-labeled probes were mixed together and hybridized to cDNA microarray slides that contained 9216 human genes (3). Hybridized slides were scanned, and the fluorescence intensities of Cy5 (sample) and Cy3 (control) for each gene spot were quantified by using a GenIII microarray scanner (Amersham Pharmacia Biotech) with Array Vision software (Imaging Research, Inc.). Each slide contained 52 housekeeping genes to normalize the signal intensities of the fluorescent dyes. The intensities of Cy5 and Cy3 were adjusted so that the mean Cy5 and Cy3 intensities of probe cDNA binding to the housekeeping genes were equivalent.

Classification of Anticancer Drugs According to Drug Activity Pattern Against Human Cancer Cell Lines. A hierarchical clustering method was applied to the chemosensitivity data. Before applying the clustering algorithm, the costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked advertisement in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

1 Supported by Grant-in-Aid for Scientific Research on Priority Areas (C) from the Ministry of Education, Culture, Sports, Science and Technology, Japan.
2 To whom requests for reprints should be addressed, at Division of Molecular Pharmacology, Cancer Chemotherapy Center, Japanese Foundation for Cancer Research, 1-37-1 Kami-Ikebukuro, Toshima-ku Tokyo 170-8455, Japan. Phone: 81-3-5394-4068; Fax: 81-3-3918-3716; E-mail: yamori@ims.u-tokyo.ac.jp.
3 The abbreviations used are: NCI, National Cancer Institute; GI50, drug concentration required for 50% growth inhibition; topo, DNA topoisomerase; TYMS, thymidylate synthetase.

Received 7/2/01; accepted 12/1/01.
the GI_{50} values were log transformed, and the absolute values \((\log GI_{50})\) were used for correlation analysis. Correlations were assessed by the Pearson correlation coefficient as described previously (2, 8). Analyses were performed using “Gene Spring” software (Silicon Genetics).

Classification of Human Cancer Cell Lines According to Gene Expression Profiles. A hierarchical clustering method was applied to the gene expression data. To obtain reproducible clusters, we selected only the 991 genes that passed the cutoff filter \([control Cy3 signals were >50,000 relative fluorescent units in >80\% of cases, i.e., 32 of 39 cell lines examined; the fluorescence ratio (Cy5:Cy3) was greater than the mean ratio by at least 5-fold in at least 3 of 39 cell lines]. Analysis was performed using Gene Spring. Before applying the clustering algorithm, the fluorescence ratio for each spot was log transformed \((\log \text{Cy5:Cy3})\), and the data for each sample centered to remove experimental biases. Correlations were assessed by the Pearson correlation coefficient as described (9, 10).

Correlation Analysis between Gene Expression Profiles and Chemosensitivity Profiles. We calculated the degree of similarity between drug activity and gene expression pattern using the Pearson correlation coefficient by the following formula:

\[
r = \frac{\sum (x_i - \bar{x}) (y_i - \bar{y})}{\sqrt{\sum (x_i - \bar{x})^2 \sum (y_i - \bar{y})^2}}
\]

where \(x_i\) represented the log expression ratio \((\log \text{Cy5:Cy3})\) of gene \(x\) in cell \(i\), whereas \(y_i\) was the log sensitivity \((\log GI_{50})\) of cell \(i\) to drug \(y\). \(x_m\) represented the mean of the log expression ratio of gene \(x\), and \(y_m\) represented the mean sensitivity \((\log GI_{50})\) of the drug. In this analysis, we selected genes that passed the cutoff filter \(\text{signal intensities were >25,000 relative fluorescent units or signal/noise ratios were >3 in either Cy3 or Cy5 in >80\% of cases, i.e., 32 of 39 cell lines examined}\). We then selected genes with expression patterns that showed significant correlation to drug activity patterns. A significant correlation was defined as a \(r < 0.05\) and a slope of the regression line >1.5, where the difference of the \(\log GI_{50}\) values between the most and the least sensitive cell lines was fixed as 1.

Clustering Analysis of Drug and Gene Profiles on the Basis of Pearson Correlation Coefficients between Drugs and Genes. We performed clustering analysis on the drugs and genes on the basis of the Pearson correlation coefficients, as described previously (10). We used all 1071 genes that passed the selection criteria described in the previous section for at least 1 of 55 drugs. The algorithm used to calculate the correlation between drug \(a\) and drug \(b\) was the standard correlation coefficient by the following formula:

\[
r = \frac{\sum a_i b_i}{\sqrt{\sum a_i^2 \sum b_i^2}}
\]

where \(a_i\) represented the Pearson correlation coefficient between drug \(a\) and gene \(i\), whereas \(b_i\) was the coefficient between drug \(b\) and gene \(i\).

Similarly, the algorithm used to calculate the correlation between gene \(c\) and gene \(d\) was the standard correlation coefficient by the following formula:

\[
r = \frac{\sum c_i d_i}{\sqrt{\sum c_i^2 \sum d_i^2}}
\]

where \(c_i\) represented the Pearson correlation coefficient between gene \(c\) and drug \(i\), whereas \(d_i\) was the coefficient between gene \(d\) and drug \(j\).

RESULTS

Developing Gene Expression and Chemosensitivity Databases Using 39 Human Cancer Cell Lines. We examined the growth inhibitory effect of 55 current anticancer drugs (Table 1) on 39 human cancer cell lines used to evaluate the efficacy of novel anticancer compounds (2). The sensitivity of each of the 39 cell lines to each drug was assessed by GI_{50}. The GI_{50} values were log transformed, and the absolute values \((\log GI_{50})\) were used for further analysis. Hierarchical clustering was performed on the 55 anticancer drugs based on their effect on the 39 cell lines (Fig. 1). As a result, the 55 drugs were classified into several clusters, each consisting of drugs with similar modes of action, e.g., one cluster included topo I inhibitors, such as camptothecin, irinotecan, and SN-38. The second cluster consisted of doxorubicin and other anthracycline compounds. 5-fluorouracil and its derivatives also clustered into a single group. Interestingly, actinomycin D, which is known not to act on tubulin, clustered with tubulin binders, including taxanes and Vinca alkaloids, suggesting actinomycin D might partly share the mode of action with these drugs. Indeed, both actinomycin D and Vinca alkaloids were shown previously to inhibit RNA synthesis in the cells. These results indicated that our system using the 39 cancer cell lines was able to classify drugs on the basis of mechanism of action. On the other hand, clustering analysis performed on the cancer cell lines according to chemosensitivity data did not always reflect the tissue of origin, in agreement with previous findings (10).

We then performed cDNA microarray analysis to investigate the expression profiles of 9216 genes in each of the 39 cell lines. The expression of each gene was assessed by the ratio of expression level in the sample against a universal control, and the values log trans-
formed before analysis [$\log_2$ (sample)/(control)]. We then applied the hierarchical clustering method to the cell line data. Cell lines with the same tissue of origin tended to form clusters, except for breast and ovarian cancers (Fig. 2). We examined the expression profiles of the cell lines NCI-H23, OVCAR3, OVCAR5, and OVCAR8 twice using independent mRNA preparations and confirmed that the four cell lines clustered very closely with each other, indicating the reproducibility of our experimental procedure (data not shown).

**Correlation Analysis between Drugs and Genes Using an Integrated Database of Gene Expression and Chemosensitivity.** To screen for genes that may be involved in chemosensitivity, we integrated the two databases and performed correlation analysis between the gene expression and drug sensitivity datasets. Comprehensive calculations for Pearson correlation coefficients were performed on the gene expression and drug sensitivity patterns of the 39 cell lines. Genes were selected that exhibited significant correlations that satisfied the following criteria: a $P$ of the correlation $<0.05$ and a slope of the regression line $>1.5$, where the difference of the $\log_{10} GI_{50}$ values between the most and the least sensitive cell lines was fixed as 1. As a result, different sets of genes were extracted with respect to each of the 55 drugs tested (data not shown). We then examined for genes that were associated with $\geq10$ of the 55 drugs.

**Fig. 1.** Two-dimensional hierarchical clustering was applied to growth inhibitory activity data of 55 anticancer drugs determined in 39 cell lines. Whereas drugs with similar mechanisms of action tended to cluster together, cell lines from the same tissue of origin did not. Cell line names are colored to reflect the tissue of origin. The tissue of origin of each cell line is described in the abbreviated symbols: LU: lung cancer; CO: colorectal cancer; GA: gastric cancer; OV: ovarian cancer; BR: breast cancer; GL: glioma; RE: renal cancer; ME: melanoma; PR: prostate cancer. Colors on the imaging map represent the relative sensitivity of the cell line against the drug. Numbers beside the drug names refer to the difference in $\log_{10} GI_{50}$ from the mean $\log_{10} GI_{50}$ for each drug, e.g., the cell line with 3.0 (in red) represents 1000-fold more sensitivity than the mean.

**Fig. 2.** Hierarchical clustering was applied to cell lines on the basis of expression data from a set of 991 cDNAs measured across 39 cell lines. The 991 cDNAs were selected from a total of 9216 genes by criteria described in “Materials and Methods.”
and found 50 genes that were significantly correlated to sensitivity to a relatively wide range of anticancer drugs (Fig. 3). Aldose reductase (AKR1B1), which catalyzes the conversion of glucose to sorbitol (11), was most commonly associated with drug sensitivity, revealing a significant correlation with 24 drugs. Damage-specific DNA binding protein 2 (DDB2), involved in DNA repair triggered by UV radiation (12), showed a positive correlation to 20 drugs. These genes were suggested to be common predictive markers of chemosensitivity. LIM domain kinase 2 (LIMK2), involved in actin skeleton remodeling (13), showed a negative correlation to 18 drugs, suggesting that LIMK2 may be a common
Fig. 4. Two-dimensional clustering analysis of genes and drugs on the basis of Pearson correlation coefficients (see “Materials and Methods”). Each row, a drug; each column, a gene. Colors are same as used in Fig. 3. As for clustering analysis based on drug activity data, drugs with similar modes of action clustered.
Fig. 5. Gene sets that commonly correlated with drugs with similar mechanisms of action. Colors are same as used in Fig. 3. The drugs examined were as follows: camptothecin and its derivatives irinotecan and SN-38 (A); bleomycin and its derivative peplomycin (B); anthracycline compounds doxorubicin, epirubicin, and daunorubicin (C); and 5-fluorouracil and its derivatives carmofur, tegafur, and doxifluridine (D). We selected genes with common significant correlations to two of two drugs (B) or two or more drugs of three (A and C) or four (D).
predictive marker of drug resistance. Interestingly, whereas overall profiles of gene expression in cancer cells reflected their tissues of origin, these genes are not strongly associated with tissue of origin (data not shown).

Correlation of Gene Expression and Drug Sensitivity on the Basis of Pearson Correlation Coefficient between Genes and Drugs. To clearly identify correlations between gene expression profiles and the sensitivity to anticancer drugs, we applied a hierarchical clustering method on both drugs and genes, based on calculations of Pearson correlation coefficients between drug efficiency and gene expression (Fig. 4). This data mining method was first developed by Scherf et al. (10, 14). We used 1,071 genes that revealed significant correlations, by the criteria mentioned above, to at least one drug (see “Materials and Methods,” data not shown). Over 50,000 (1,071 × 55) correlations were calculated and clustered. Similar to the clustering analysis performed using drug sensitivity data, sets of drugs with similar mechanisms of action tended to cluster with each other; however, some clusters were reorganized (Figs. 1 and 4). The result indicated that the correlating gene sets tended to overlap with respect to drugs with similar mechanisms of action.

Putative Genes Involved in Chemosensitivity. We then searched for genes that correlated with clusters of drugs with similar mechanisms of action. For the 5-fluorouracil derivatives, we identified genes that revealed significant correlations with at least two of the four drugs, 5-fluorouracil, carmofur, tegafur, and doxifluridine, as shown in Fig. 5D. Among the 51 genes that showed a negative correlation,
the gene encoding cyclin C (CCNC) exhibited a broad negative correlation, not only with 5-fluorouracil derivatives but also with topo inhibitors, anthracyclines, antifolates, and tubulin binders. In contrast, the genes coding KIAA0097 protein and survivin (BIRC5) showed specific correlation only to fluoropyrimidines. Genes with positive correlations included some aldo-keto reductase family members (AKR1C1, AKR1C3, and AKR1B11), two aldehyde dehydrogenases (ALDH1 and ALDH3), and galec tin 4 (LGALS4, in duplicate).

We performed similar analyses with respect to other sets of drugs, such as topo I inhibitors (camptothecin, irinotecan, and SN-38; Fig. 5A), bleomycin derivatives (bleomycin and peplomycin; Fig. 5B), and anthracyclines (doxorubicin, epirubicin, and daunorubicin; Fig. 5C). As a result, we generated different sets of genes that revealed positive and negative correlations with respect to different clusters of drugs. Of these, topo I inhibitors, bleomycin derivatives, and anthracyclines closely clustered with each other on the basis of both drug activity and Pearson correlation coefficient, suggesting these compounds act by similar mechanisms (Figs. 1 and 4), e.g., genes encoding 14-3-3 σ (SFN), LIM domain kinase 2 (LIMK2), and cathepsin H (CTSH) commonly showed negative correlations, whereas genes encoding DDB2 (DDB2) and the all-fused gene from chromosome 1q (AF1Q) revealed positive correlations (Fig. 5, A–C). However, we also observed some differences, e.g., keratins (KRT7–8 and -19) correlated with camptothecins and bleomycin derivatives but not with anthracyclines, whereas expression of the gene encoding transducer of ErbB2 1 (TOBI) positively correlated with anthracine but not with bleomycin or camptothecins. Our results suggested that drugs with similar mechanisms of action shared sets of genes involved in cancer cell susceptibility and that these gene sets varied with respect to clusters of drugs with similar mechanisms of action.

DISCUSSION

In this study, we investigated the gene expression profiles of 39 human cancer cell lines that were pharmacologically characterized on treatment with various anticancer drugs, using a cDNA microarray system consisting of 9216 genes. In conjunction with chemosensitivity data, we identified genes expressed in the 39 cell lines with expression patterns that correlated significantly with the susceptibility profiles of each of the 55 anticancer drugs evaluated. Positively correlating genes are likely to reflect chemosensitivity as the higher the expression level of these genes, the lower the GI50. Similarly, genes that showed negative correlations are likely to reflect chemoresistance. Thus, the expression levels of these genes may be useful as predictive markers of drug effectiveness.

Our database, comprising both gene expression data and drug activity data for the same set of cell lines, was first developed by Ross et al. and Scherf et al. (9, 10) using 60 human cancer cell lines (NCI60). These studies examined gene expression profiles in 60 cell lines that were pharmacologically characterized on treatment with various kinds of anticancer drugs. The number of cell lines used in the present study was 39. Of these, 9 cell lines (6 derived from gastric cancers and 3 from breast cancers) were not included in the NCi60 panel (4). Using this different set of 39 cell lines, we performed hierarchical clustering with respect to 55 anticancer drugs on the basis of growth inhibition and Pearson correlation coefficients between drugs and genes. As shown in Figs. 1 and 4, drugs with similar mechanisms of action clustered most of the time, in agreement with results of an earlier study that used a different set of cell lines (10). Moreover, we have shown previously that the mode of action of a novel compound can be predicted by examining its growth inhibitory activities against the panel of 39 cell lines (2, 8). This indicated that our cell line panel had sufficient power to classify drugs according to mode of action. The previous study by Scherf et al. (10) showed expected correlations, such as that between 5-fluorouracil and dihydropyrimidine dehydrogenase (DPYD). A moderately negative correlation between 5-fluorouracil and TYMS was demonstrated in our study ($r = -0.29, P < 0.1$). In addition, a stronger negative correlation between 5-fluorouracil derivative camptothecin and TYMS was also observed ($r = -0.38, P < 0.01$; data not shown). Furthermore, positive correlations between the DNA topo II inhibitor etoposide and DNA topo II α (TOP2A, $r = 0.39, P < 0.05$) and β (TOP2B, $r = 0.29, P < 0.1$) were also found (data not shown). Although the Pearson correlation coefficients were not high, together these moderate correlations might be sufficient as the sensitivity of cancer cells to anticancer drugs appears not to be determined by the expression of a single gene. Clustering analysis of cell lines revealed that overall profiles of gene expression in cancer cells reflected their tissues of origin (Fig. 2). Therefore, some of the retrieved genes preferentially expressed in cells derived from specific tissues, e.g., keratin genes related to epithelial cell type (data not shown). Similarly, some of the drugs used in our study tended to show tissue-oriented efficacy (Fig. 1). Therefore, some of the genes reflecting cells’ tissue of origin correlating with chemosensitivity might be associated with sensitivity to such drugs. On that occasion, the correlation should be validated within each set of cell lines derived from the same tissues. On the other hand, there was a substantial population of genes that was not strongly associated with tissue of origin, including AKR1B1, LIMK2, and DDB2 (data not shown). These genes are conceivably good candidates for predictive markers of drug efficacy.

Clustering analysis of the drugs on the basis of Pearson correlation coefficients between drug activity and gene expression levels revealed that drugs with similar modes of action clustered into the same groups and that the sets of chemosensitivity-associated genes were similar between each drug within a group (Fig. 4). Thus, we were able to retrieve genes that commonly correlated within each of the groups of drugs with similar functions (Fig. 5, A–D, data not shown), e.g., we identified the genes encoding survivin (BIRC5) and C-IAP1 of apoptosis1 (BIRC2) that revealed negative correlations with 5-fluorouracil derivatives, although survivin showed either no significant negative correlations or moderately positive correlations to the other genotoxic anticancer drugs (Fig. 5D). The inhibitor of apoptosis family of proteins, including survivin, has been shown to play important roles in the suppression of apoptosis and is conceivably a chemoresistance factor (15, 16). Thus, the most important aspect of our analysis is that we were able to retrieve different gene sets that may be used as putative diagnostic markers for chemosensitivity prediction with respect to each class of drugs with similar mechanisms of action. The next step will be to confirm the predictive power of our findings. In a recently published study, Staunton et al. (17) identified putative predictive markers of chemosensitivity and showed the feasibility of chemosensitivity prediction by transcriptional profiling. In our current study, using a different methodology, we could narrow down the number of candidate genes from hundreds to dozens that predict chemosensitivity, although we have not completed to evaluate our findings. The validation studies using dozens of cell lines outside the panel are under way.

In summary, we have identified different sets of genes that may act as predictive markers for chemosensitivity to drugs with similar mechanisms of action. Data-mining methodologies described here and elsewhere (17) may be useful to develop systems to select suitable chemotherapies in the future. However, statistical correlations are not the proof of causal relationships between gene expression and chemosensitivity. If these causal relationships can be demonstrated experimentally, the resultant gene products may explain the mechanisms...
of anticancer drugs. In addition, to elucidate the mechanisms of anticancer drugs, it is also necessary to determine gene expression changes after administration of drugs (18). These studies will help us to discover new targets of cancer chemotherapy, as well as predictive markers for conventional drugs.

ACKNOWLEDGMENTS

We thank Dr. Jun-ichi Okutsu for helpful discussions and Hiroko Bando, Noriko Nemoto, and Noriko Sudo for the fabrication of cDNA microarray. We also thank Yumiko Nishimura, Mariko Seki, Keiko Sato, Fujiko Ohashi, Yoko Yoshida, Naohide Sunose, Sachiko Udagawa, and Akiko Kuramochi-Komi for the determination of chemosensitivity.

REFERENCES


An Integrated Database of Chemosensitivity to 55 Anticancer Drugs and Gene Expression Profiles of 39 Human Cancer Cell Lines

Shingo Dan, Tatsuhiko Tsunoda, Osamu Kitahara, et al.


Updated version
Access the most recent version of this article at:
http://cancerres.aacrjournals.org/content/62/4/1139

Cited articles
This article cites 18 articles, 9 of which you can access for free at:
http://cancerres.aacrjournals.org/content/62/4/1139.full.html#ref-list-1

Citing articles
This article has been cited by 30 HighWire-hosted articles. Access the articles at:
/content/62/4/1139.full.html#related-urls

E-mail alerts
Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.