Additional File 2: Figures S1-S17

Figure S1. Heat map and two-dimensional clustering of gene expression changes (log₂ difference in expression values between treated and untreated cell lines) of members of DNA methylation and demethylation pathways, the OCM pathway, and potential methylation target genes in the NCI-60 cell lines at 24 hours after treatment with the high concentration (5,000 nM) of 5-azacytidine. NCI-60 cell lines are represented by columns, whereas individual genes are represented by rows.

Figure S2. Changes in expression of selected genes (PCNA, GADD45A, MBD4, TDG, MTHFD1, and MTHFD2) at 2 (left panel), 6 (middle panel), and 24 hours (right panel) after treatment with the high concentration (5,000 nM) of 5-azacytidine. Horizontal right bars indicate elevated gene expression, whereas left bars decreased expression relative to cell lines untreated by drug. Colors represent different types of cancer tissues (breast, central nervous system (CNS), colon, leukemia, lung, melanoma, ovarian, prostate, and renal cancers). The scale on the bottom represents log₂ difference between expression values of treated and untreated cell lines. The scale for each microarray experiment is specific to that experiment.

Figure S3. Transcriptional changes of CTH at 2 (left panel), 6 (middle panel), and 24 hours (right panel) after treatment with high concentrations of (A) 5-azacytidine (5,000 nM); (B) doxorubicin (1,000 nM); (C) vorinostat (5,000 nM); and (D) cisplatin (15,000 nM). Additional information about data representation is provided in the legend to Fig. S2.

Figure S4. Drug-specific response patterns of expression changes of DHFR at 2 (left panel), 6 (middle panel), and 24 hours (right panel) after treatment with high concentrations of (A) 5-azacytidine (5,000 nM); (B) doxorubicin (1,000 nM); (C) vorinostat (5,000 nM); (D) paclitaxel (100 nM); and (E) cisplatin (15,000 nM). Additional information is provided in the legend to Fig. S2.

Figure S5. Heat map and two-dimensional clustering of gene expression changes of members of DNA methylation and demethylation pathways, the OCM pathway, and potential methylation target genes in the NCI-60 cell lines at 24 hours after treatment with the high concentration (1,000 nM) of doxorubicin. Individual genes are represented by rows. Cell lines are represented by columns, with the right most column representing the T-47D cell line with a distinct pattern of expression changes.

Figure S6. Changes in expression of DNMT3B at 2 (left panel), 6 (middle panel), and 24 hours (right panel) after treatment with high concentrations of (A) doxorubicin (1,000 nM); and (B) vorinostat (5,000 nM). Additional information is provided in the legend to Fig. S2.

Figure S7. Changes in expression of PCNA, GADD45A, MBD4, and MECP2 involved in DNA methylation, demethylation, and DNA repair at 2 (left panel), 6 (middle panel), and 24 hours (right panel) after treatment with the high concentration (1,000 nM) of doxorubicin. Additional information is provided in the legend to Supplementary Fig. 2. The opposite direction of expression changes in the T-47D cell line at 6 and/or 24 hours after treatment as compared to the direction of changes in the majority of other NCI-60 cell lines can be seen in the middle and right panels for each gene.

Figure S8. Changes in expression of selected OCM pathway genes (ATIC, MAT2A, MTHFS, and MTR) at 2 (left panel), 6 (middle panel), and 24 hours (right panel) after treatment with the high (1,000 nM) or low (500 nM) concentrations of doxorubicin. Additional information is provided in the legend to Supplementary Fig. 2. Upregulation of expression of the T-47D cell line at 24 hours after treatment as opposed to downregulation of the majority of other NCI-60 cell lines can be seen in the right panels for each gene.

Figure S9. Heat map and two-dimensional clustering of gene expression changes of members of DNA methylation and demethylation pathways, the OCM pathway, and potential methylation target genes at 24
hours after treatment with the high concentration (5,000 nM) of vorinostat. Additional information about data representation is provided in the legend to Fig. S1.

**Figure S10.** Changes in DNMT3A expression at 2 (left panel), 6 (middle panel), and 24 hours (right panel) after treatment with vorinostat: (A) high concentration (5,000 nM); (B) low concentration (1,000 nM). Additional information about data representation is provided in the legend to Fig. S2.

**Figure S11.** Changes in expression of APOBEC3C, TDG, MBD1, MBD3, MBD4, and MECP2 involved in DNA methylation, demethylation, and DNA repair at 2 (left panel), 6 (middle panel), and 24 hours (right panel) after treatment with the high concentration (5,000 nM) of vorinostat. Additional information about data representation is provided in the legend to Fig. S2.

**Figure S12.** Changes in gene expression of selected members of the OCM pathway (SLC19A1, FOLR1, MAT2B, MTR, ATIC, MTHFS, and MTHFD1) at 2 (left panel), 6 (middle panel), and 24 hours (right panel) after treatment with the high concentration (5,000 nM) of vorinostat. Additional information is provided in the legend to Fig. S2.

**Figure S13.** Heat map and two-dimensional clustering of gene expression changes of members of DNA methylation and demethylation pathways, the OCM pathway, and potential methylation target genes in the NCI-60 cell lines at 24 hours after treatment with the high concentration (100 nM) of paclitaxel. Additional information is provided in the legend to Fig. S1.

**Figure S14.** Changes in expression of PCNA, TDG, IDH1, and GART at 2 (left panel), 6 (middle panel), and 24 hours (right panel) after treatment with the high concentration (1,000 nM) of paclitaxel. Additional information is provided in the legend to Fig. S2.

**Figure S15.** Heat map and two-dimensional clustering of gene expression changes of members of DNA methylation and demethylation pathways, the OCM pathway, and potential methylation target genes in the NCI-60 cell lines at 24 hours after treatment with the high concentration (15,000 nM) of cisplatin. Additional information is provided in the legend to Fig. S1.

**Figure S16.** Changes in expression of selected genes (PCNA, GADD45A, MGMT, MBD1, MBD4, and USP7) involved in DNA methylation, demethylation, and DNA repair pathways at 2 (left panel), 6 (middle panel), and 24 hours (right panel) after treatment with the high concentration (15,000 nM) of cisplatin. Additional information is provided in the legend to Fig. S2.

**Figure S17.** Changes in expression of selected members of the OCM pathway (MAT2A, PEMT, MTHFD2, and MTHFD2L) at 2 (left panel), 6 (middle panel), and 24 hours (right panel) after treatment with the high concentration (15,000 nM) of cisplatin. Additional information is provided in the legend to Fig. S2.
Fig. S2. (cont.)
**ATIC**
high dose

**ATIC**
low dose

**MAT2A**
high dose

Fig. S8
MTHFS high dose

MTR high dose

MTR low dose

Fig. S8 (cont.)
Fig. S10
APOBEC3C

TDG

MBD1

Fig. S11
Fig. S12 (cont.)
Fig. S14

PCNA

TDG

IDH1

GART
PCNA

GADD45A

MGMT

Fig. S16
**MBD1**

2 hours

6 hours

24 hours

**MBD4**

2 hours

6 hours

24 hours

**USP7**

2 hours

6 hours

24 hours

Fig. S16 (cont.)
MAT2A

PEMT

MTHFD2

MTHFD2L

Fig. S17