

Additional File 2: Figures S1-S17

Figure S1. Heat map and two-dimensional clustering of gene expression changes (\log_2 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 \log_2 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.

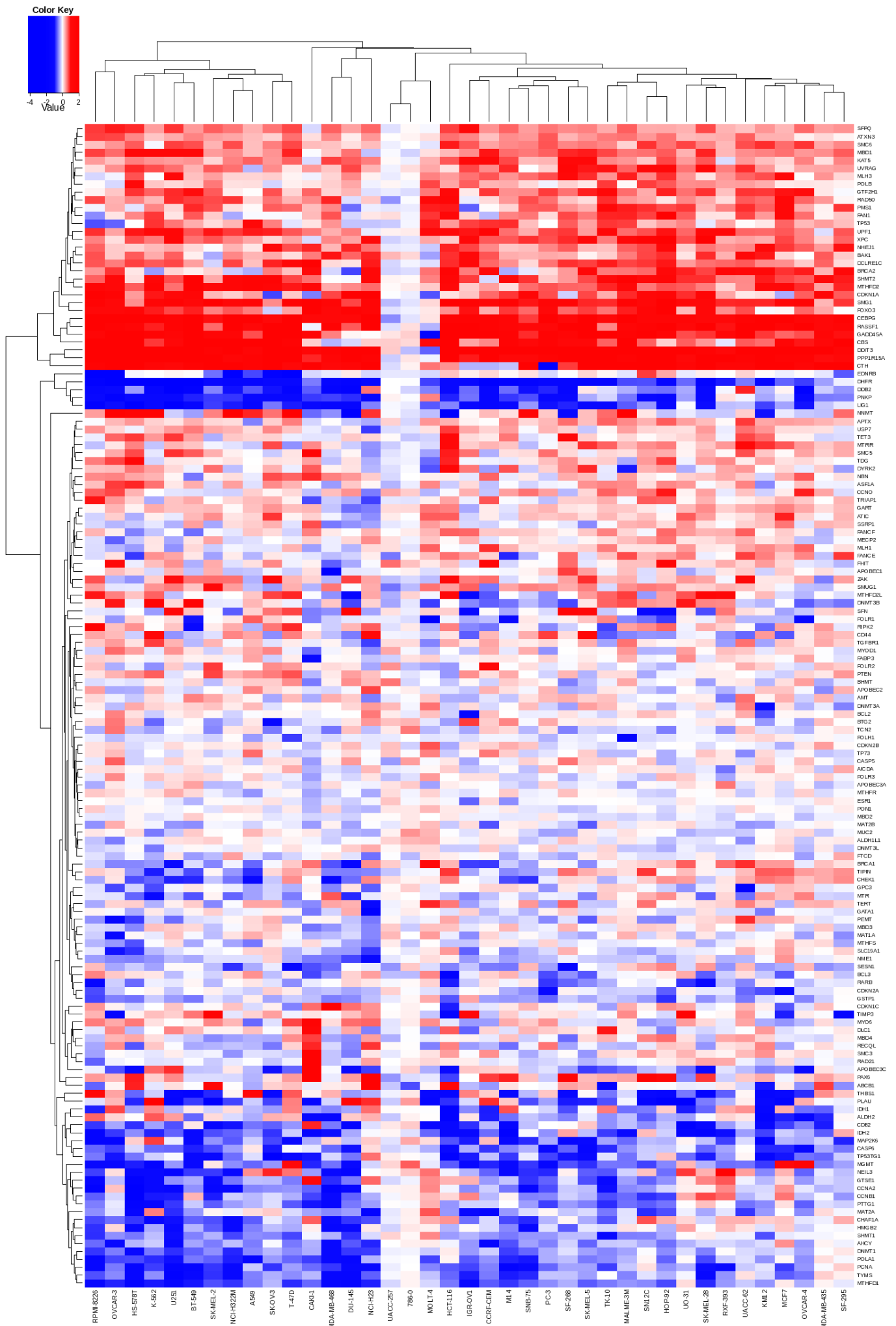
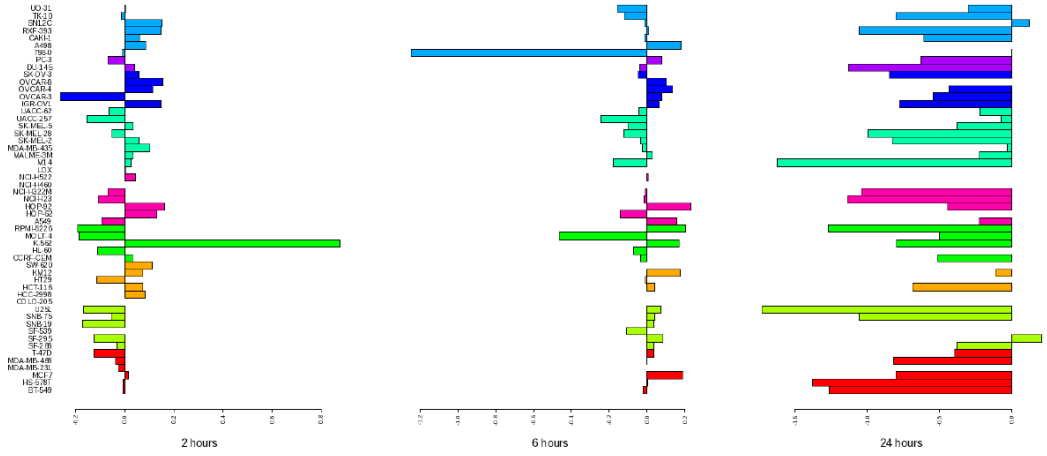


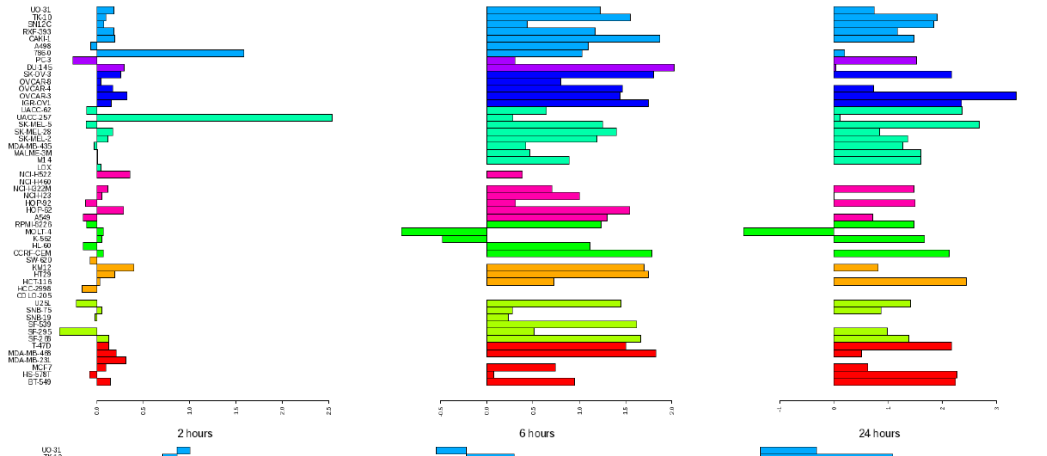
Fig. S1

BREAST COLON LEUKEMIA LUNG MELANOMA OVARIAN PROSTATE RENAL

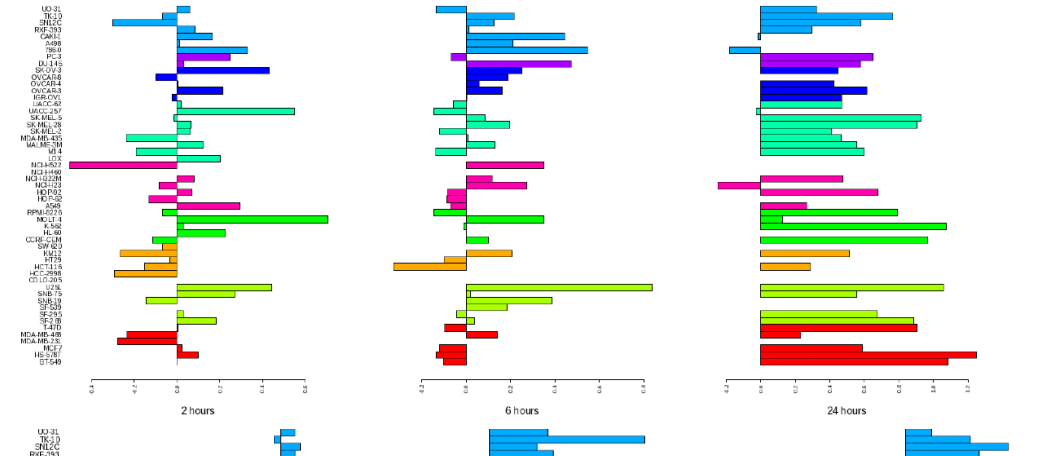
PCNA



GADD45A



MBD1



MBD4

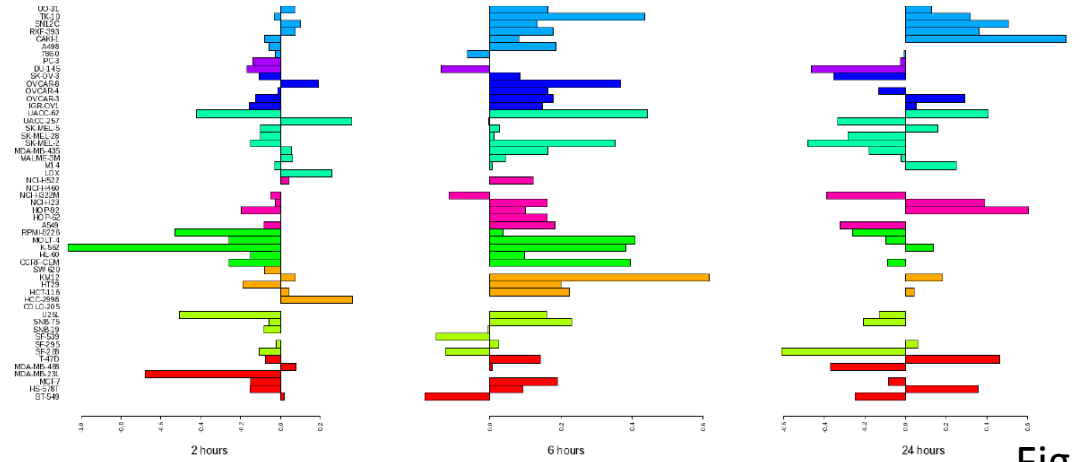
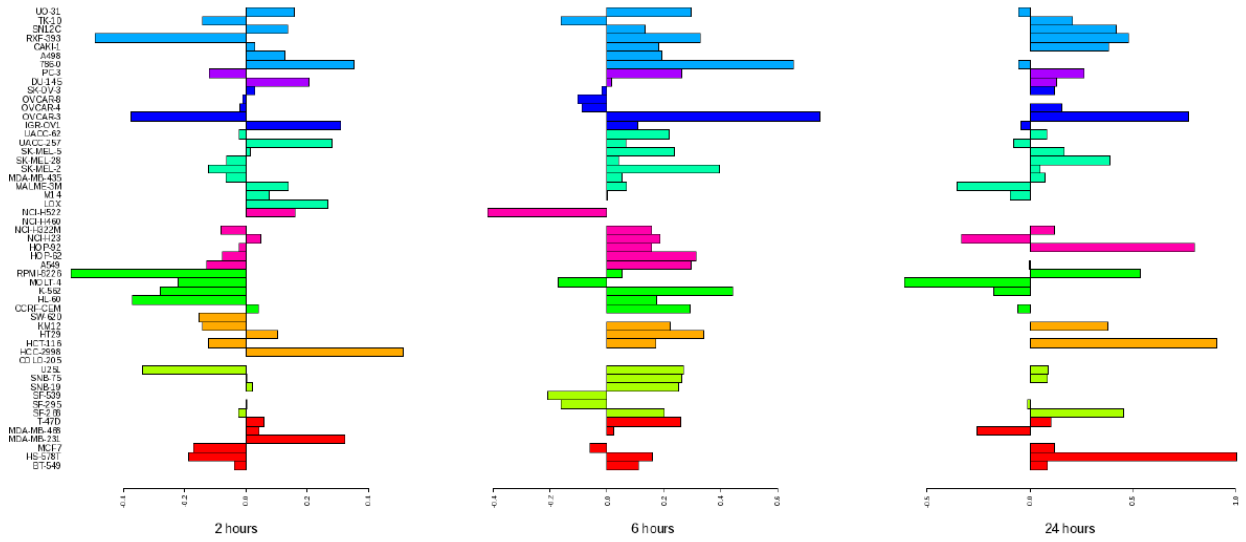


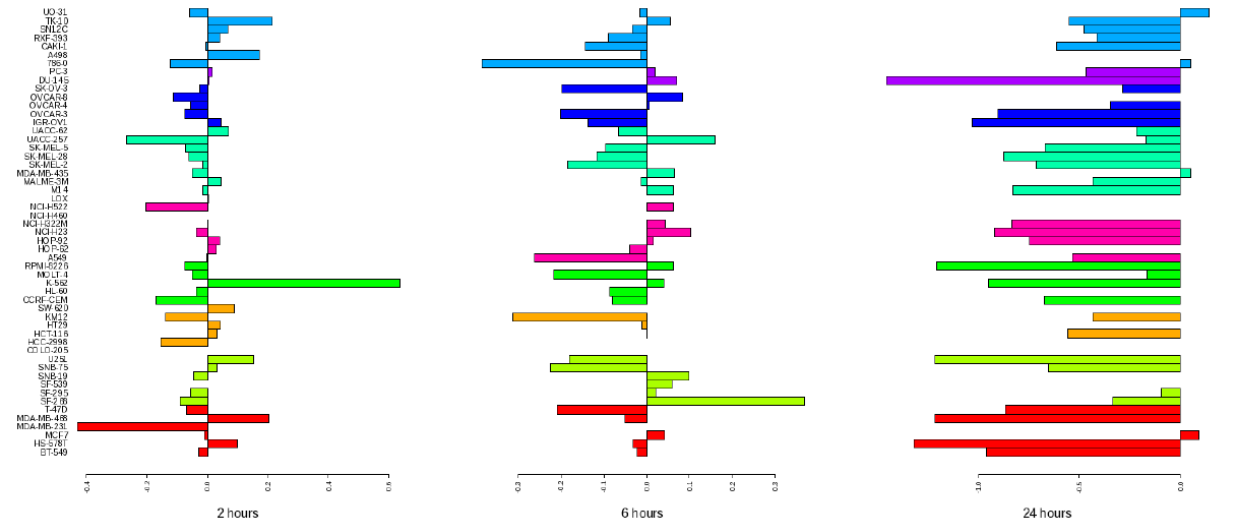
Fig. S2.

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TDG



MTHFD1



MTHFD2

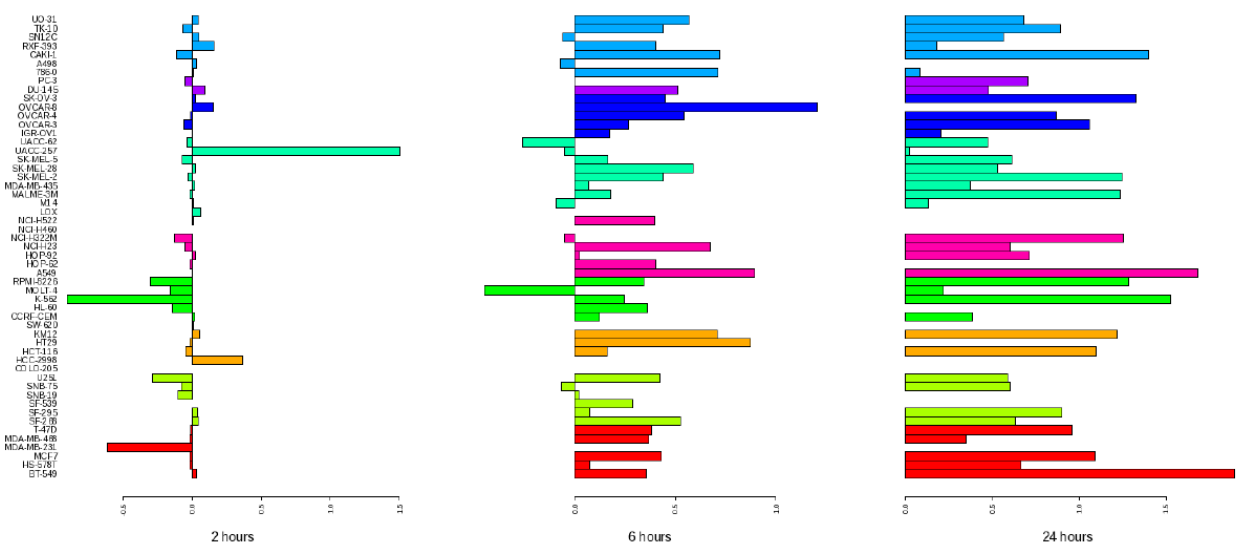
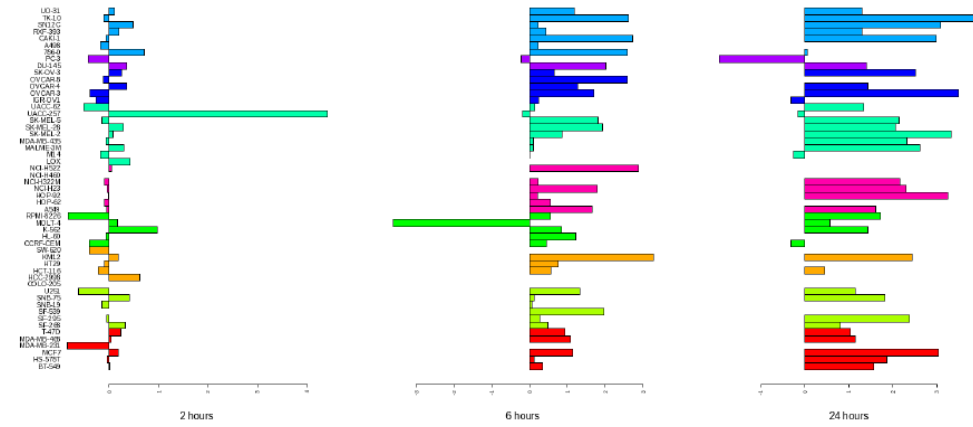
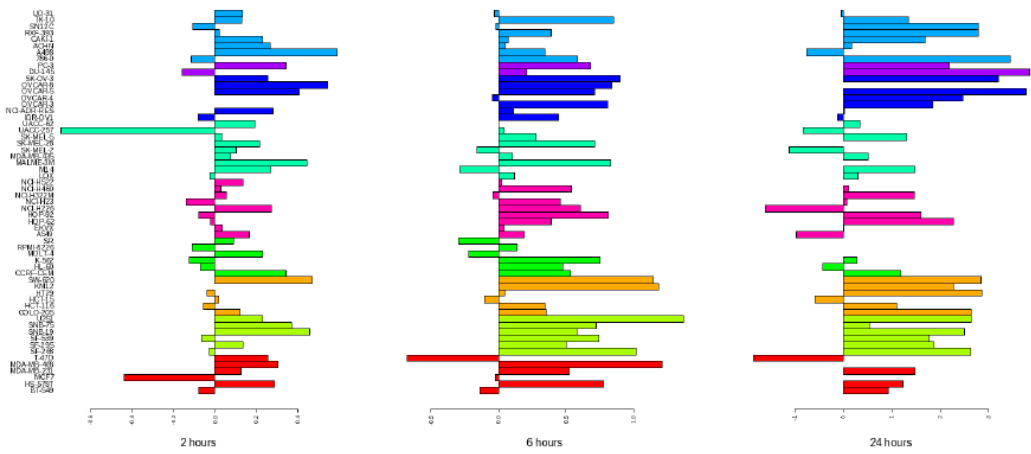


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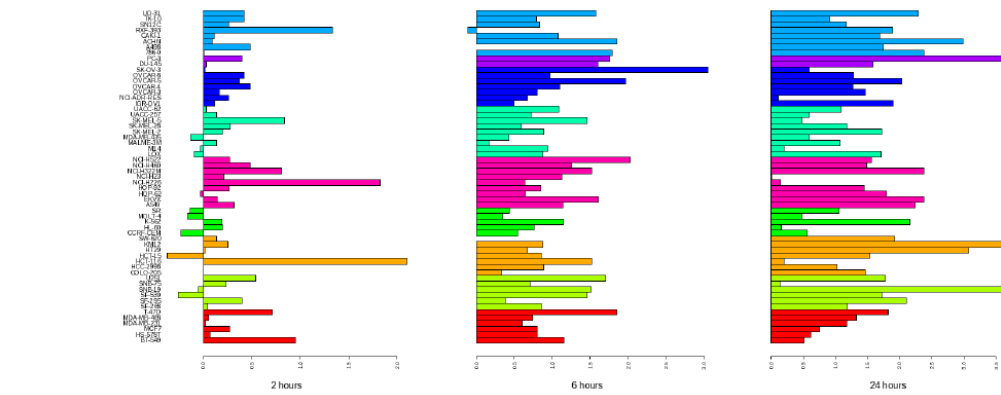
A



B



C



D

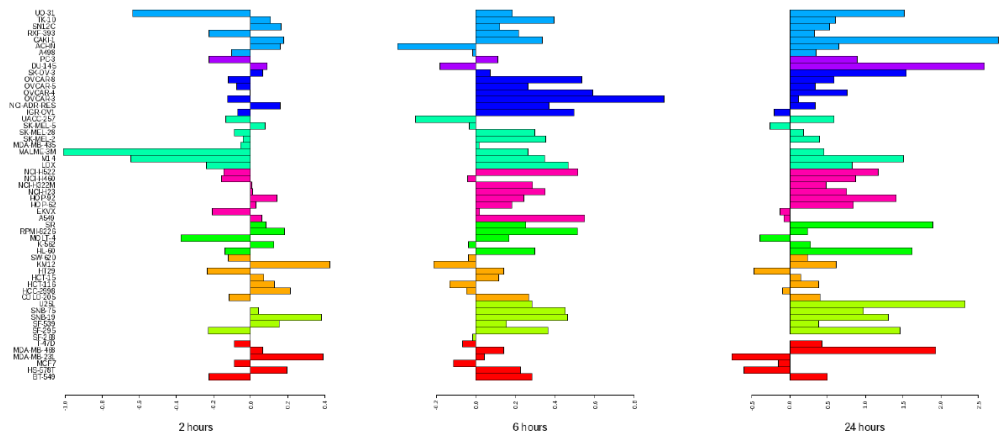


Fig. S3.

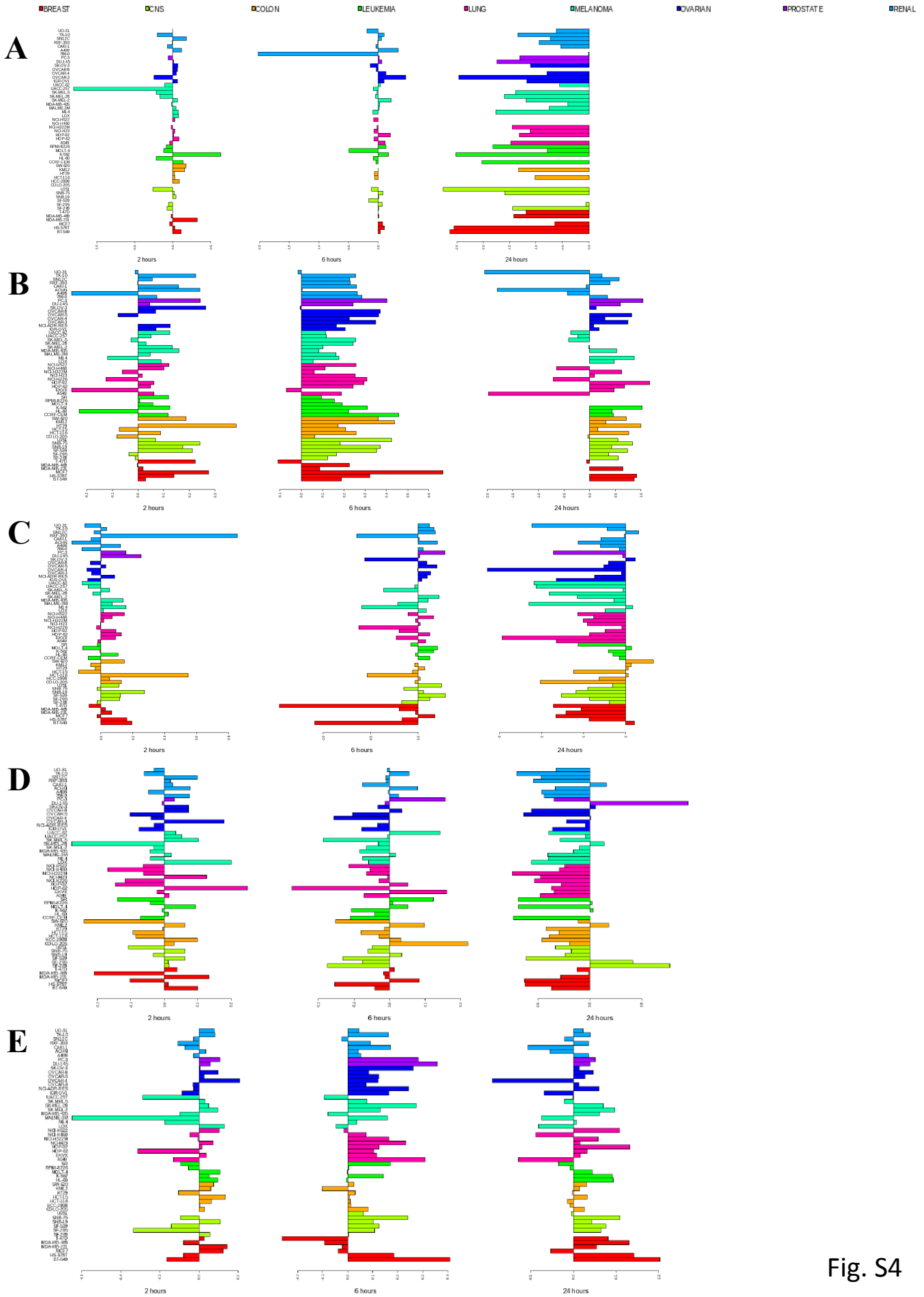


Fig. S4

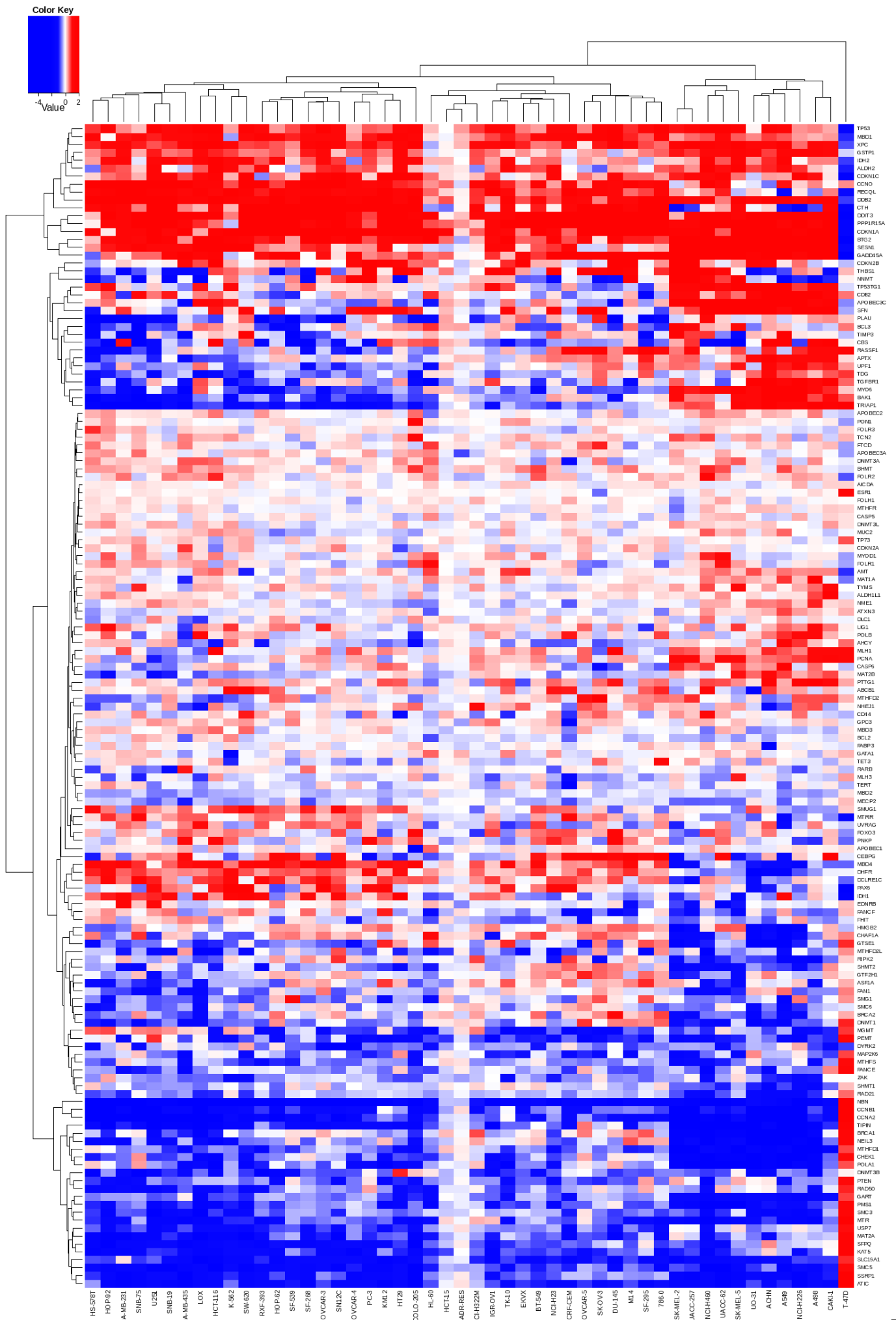


Fig. S5

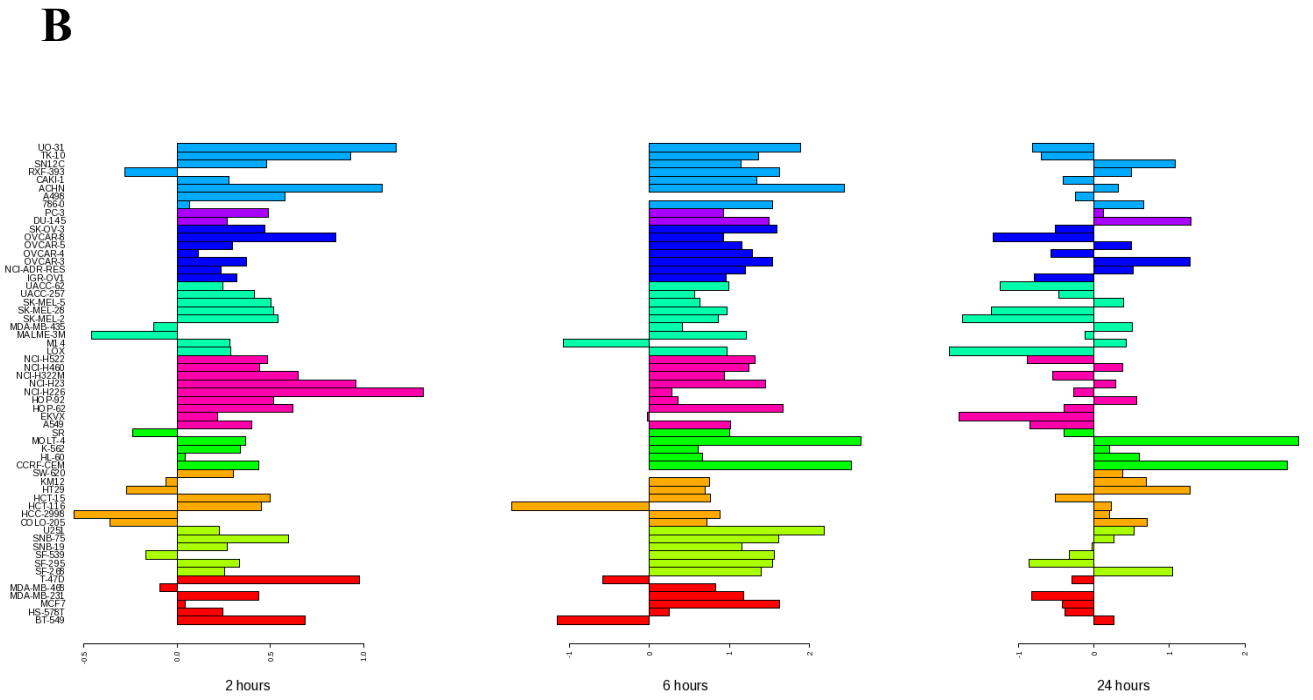
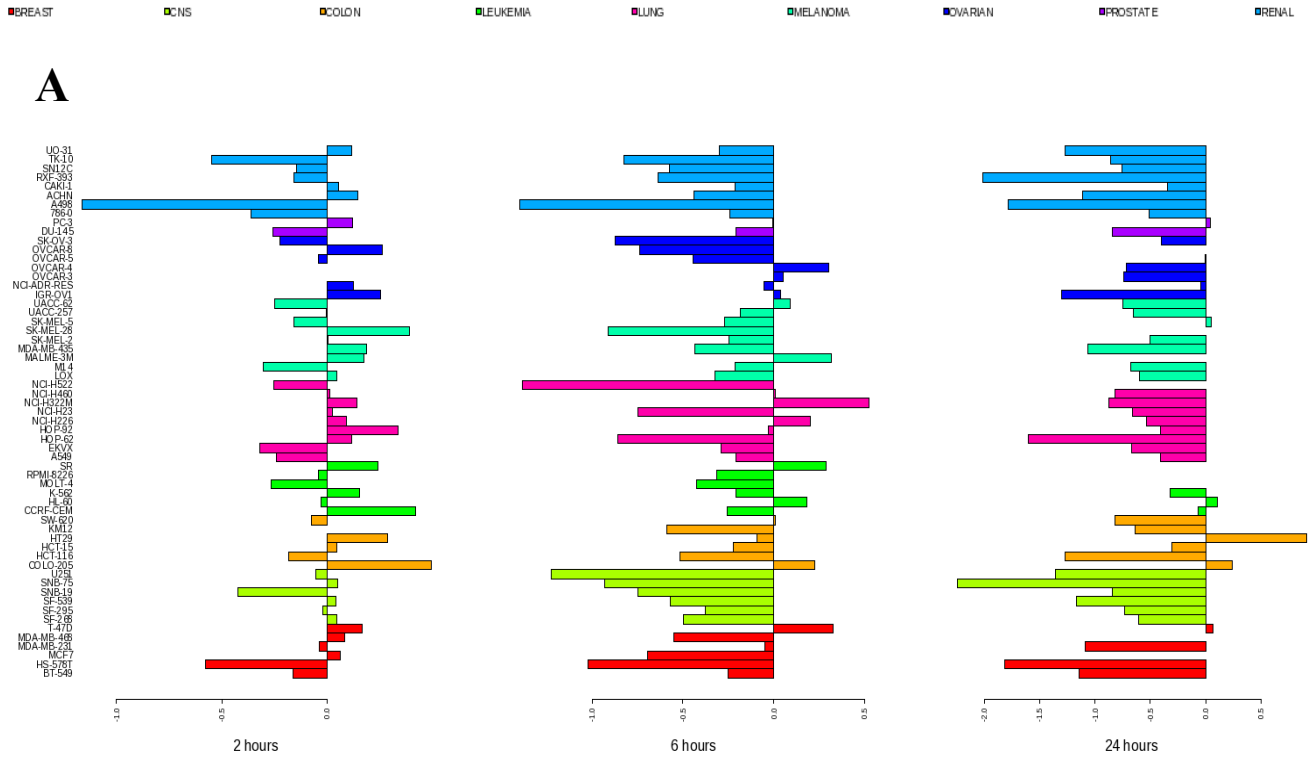
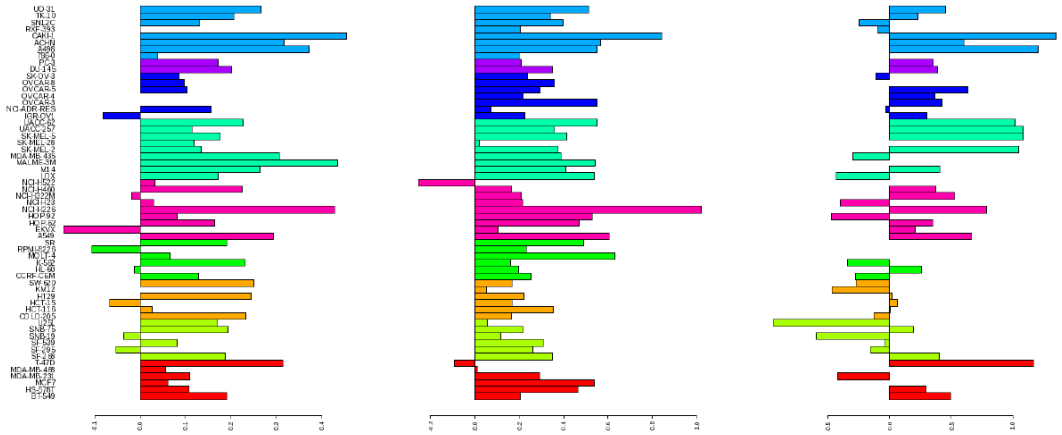


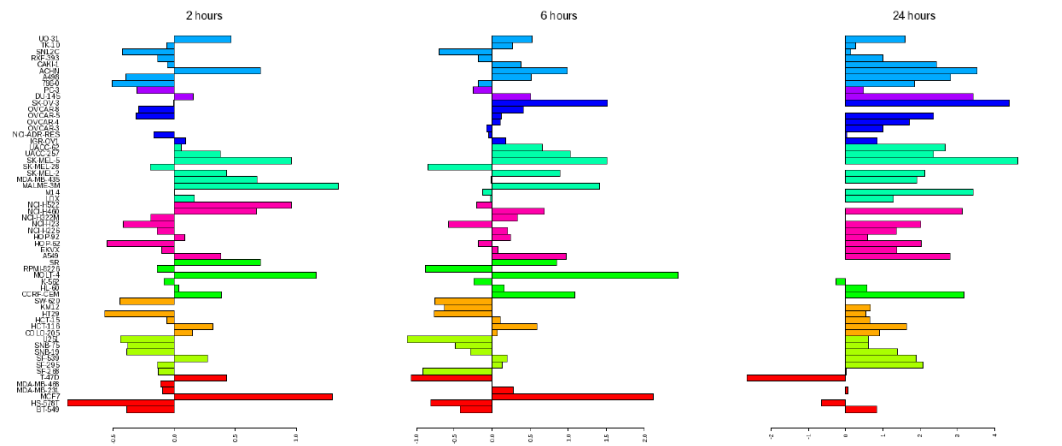
Fig. S6

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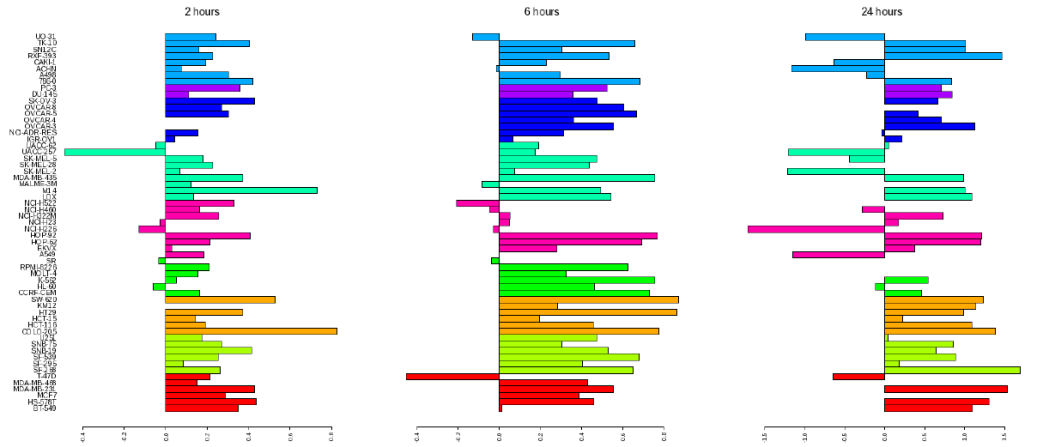
PCNA



GADD45A



MBD4



MECP2

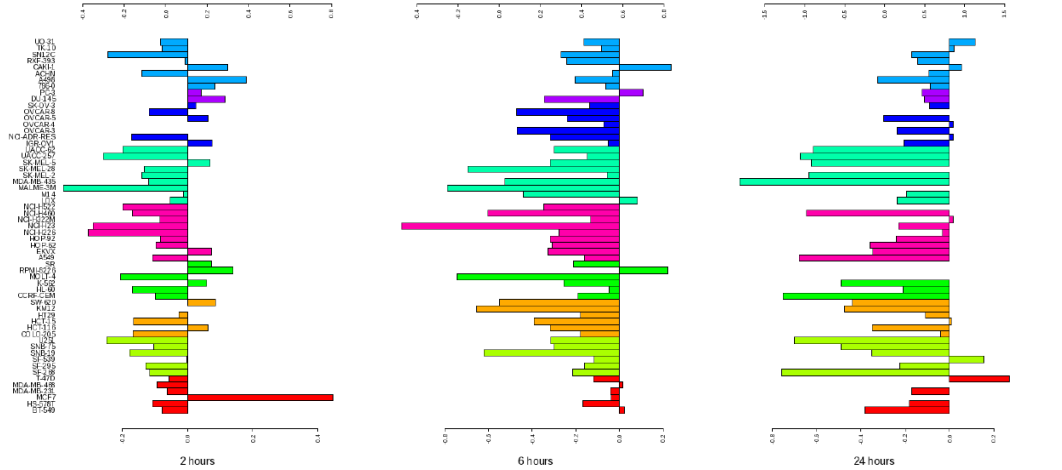
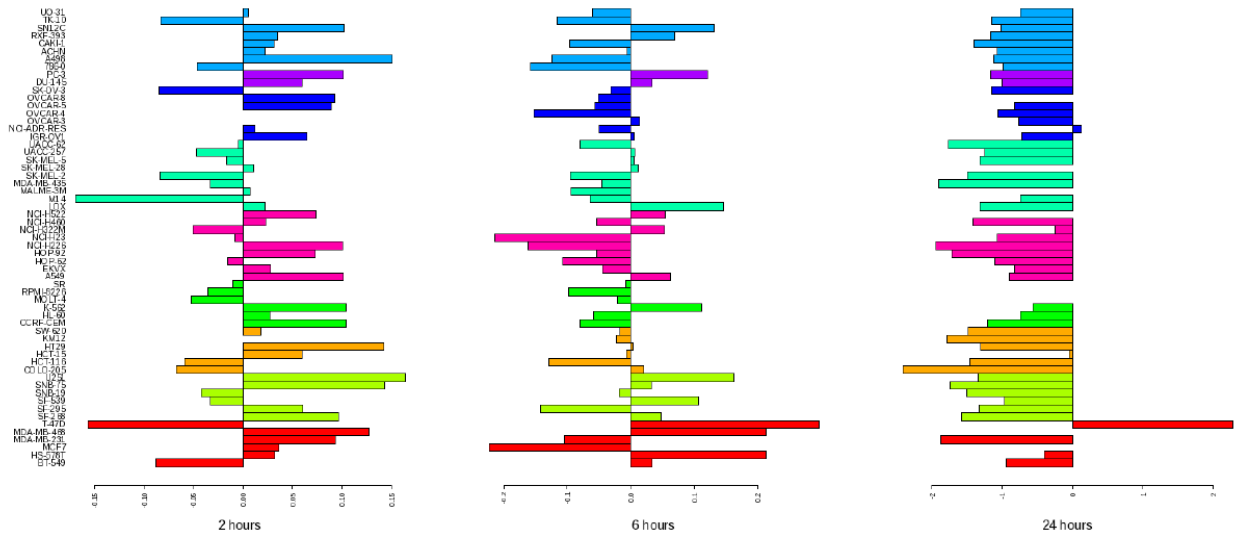


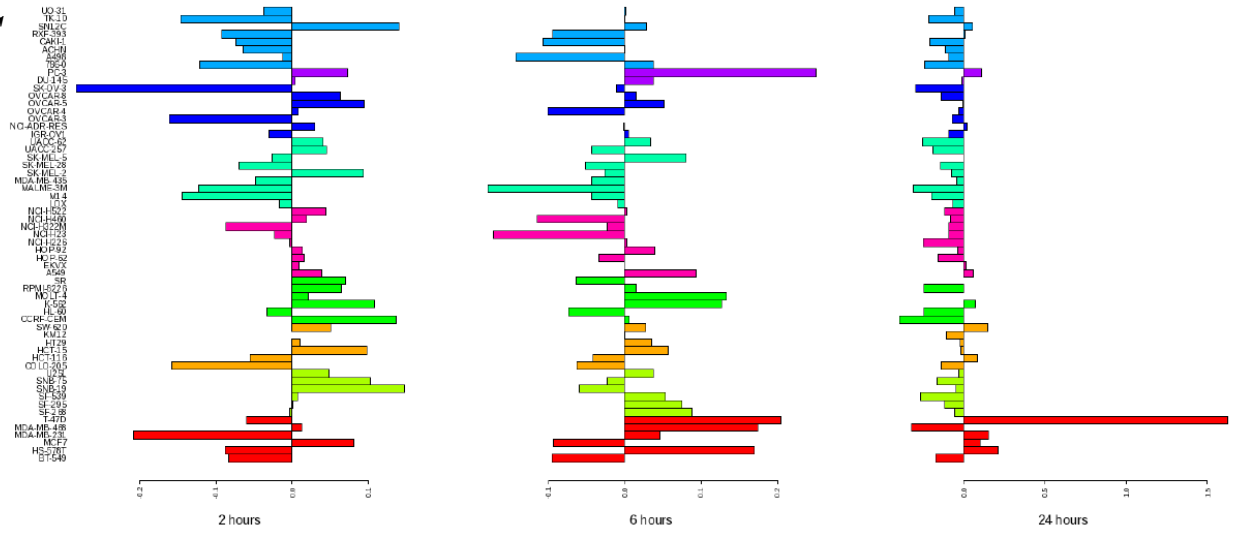
Fig. S7

■ BREAST
 ■ CNS
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 ■ LEUKEMIA
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 ■ MELANOMA
 ■ OVARIAN
 ■ PROSTATE
 ■ RENAL

ATIC
high dose



ATIC
low dose



MAT2A
high dose

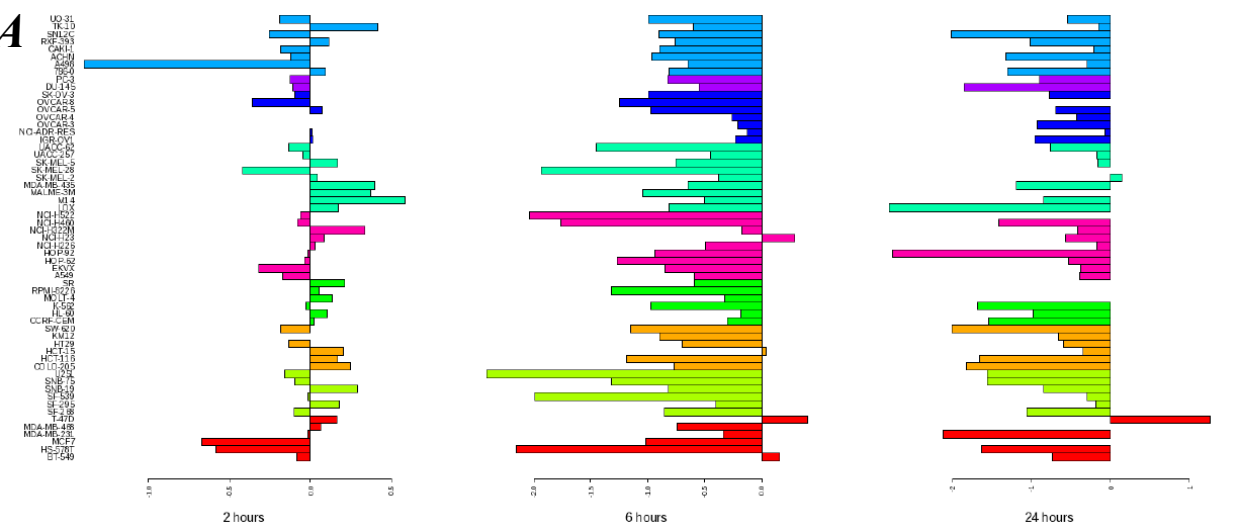
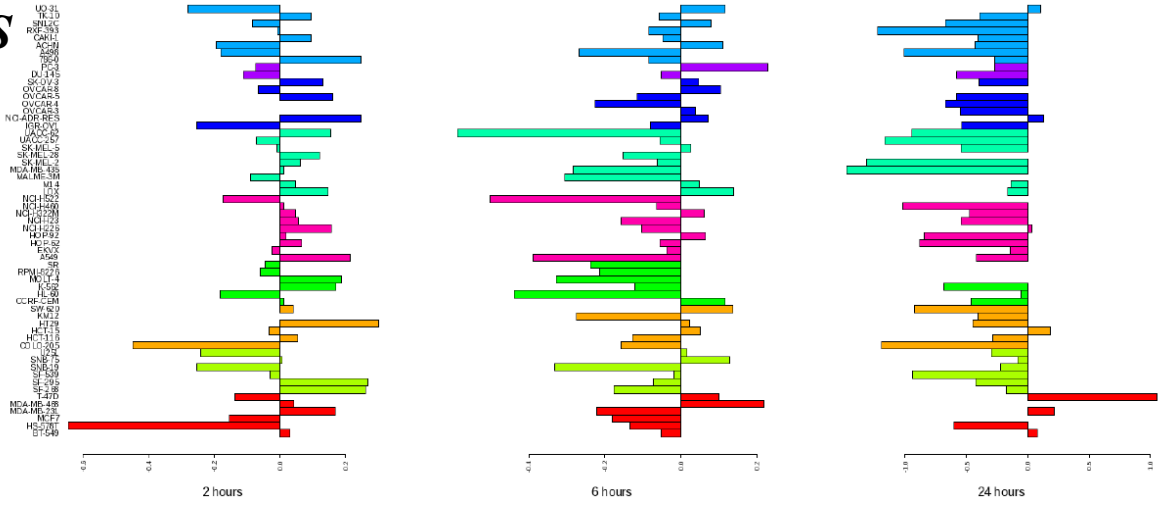


Fig. S8

■ BREAST
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 ■ MELANOMA
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 ■ RENAL

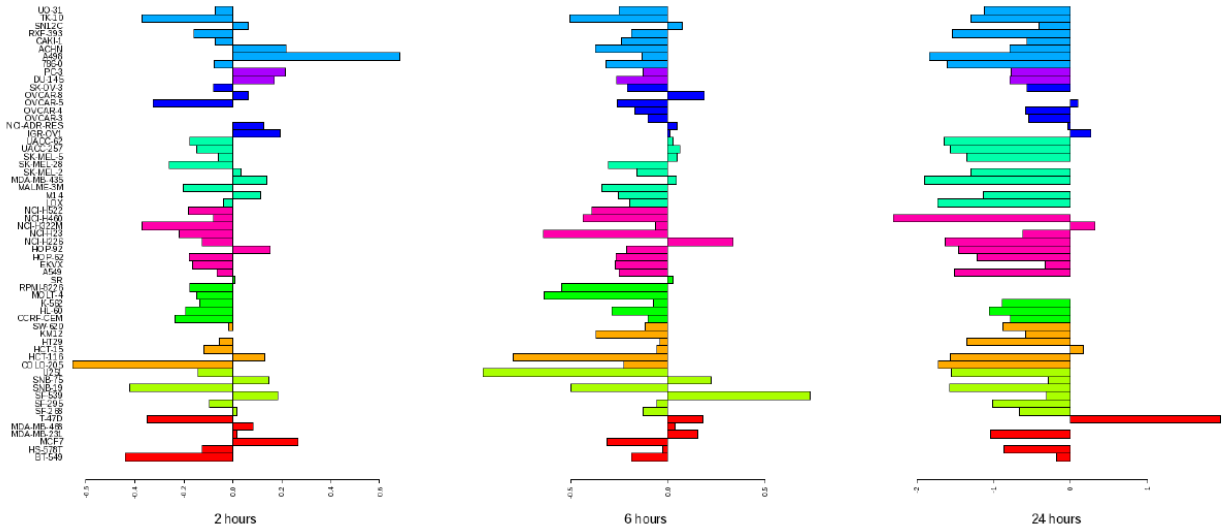
MTHFS

high dose



MTR

high dose



MTR

low dose

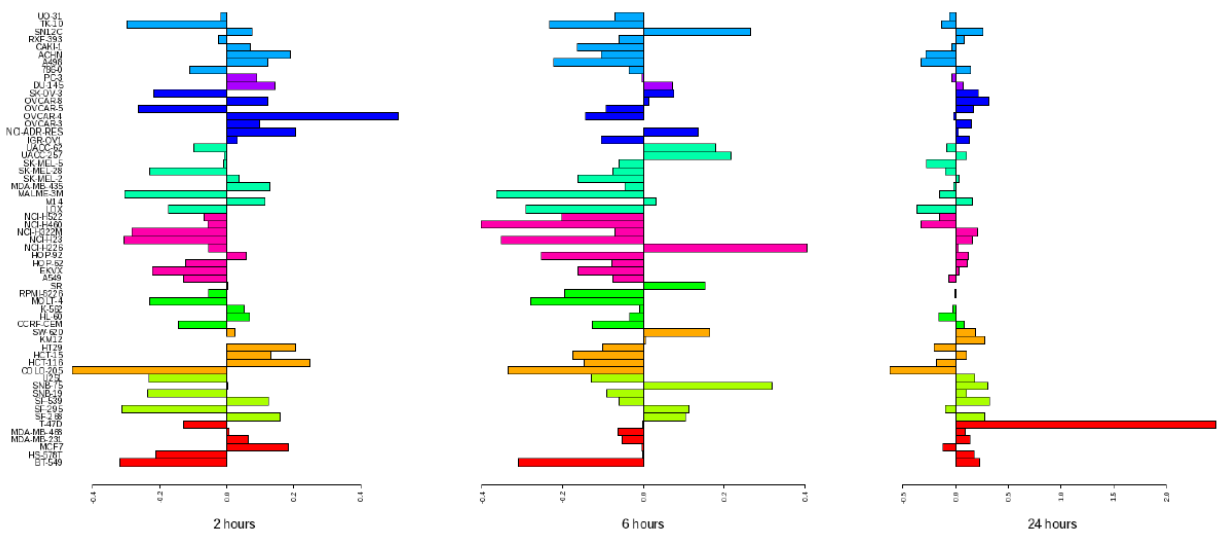


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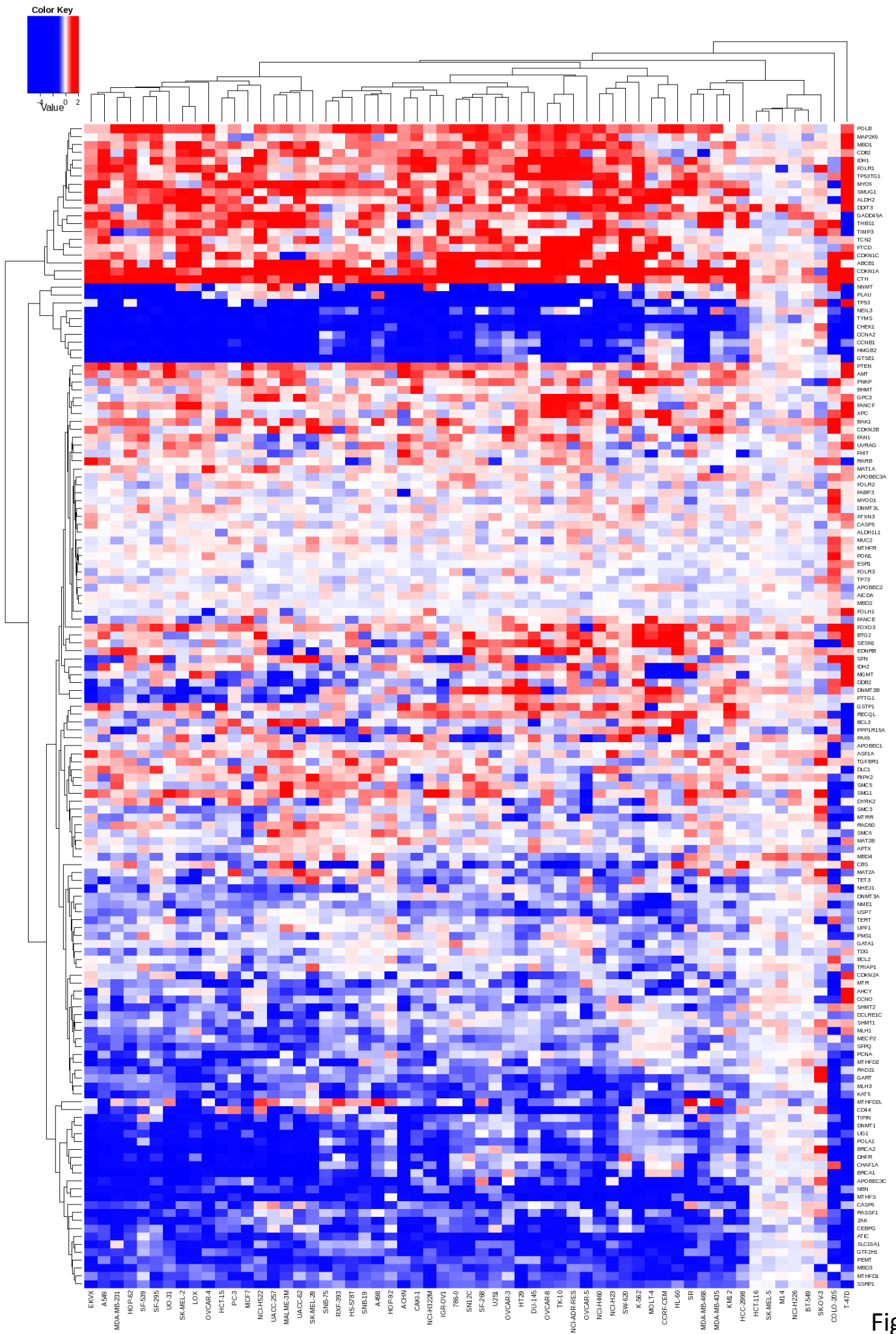


Fig. S9

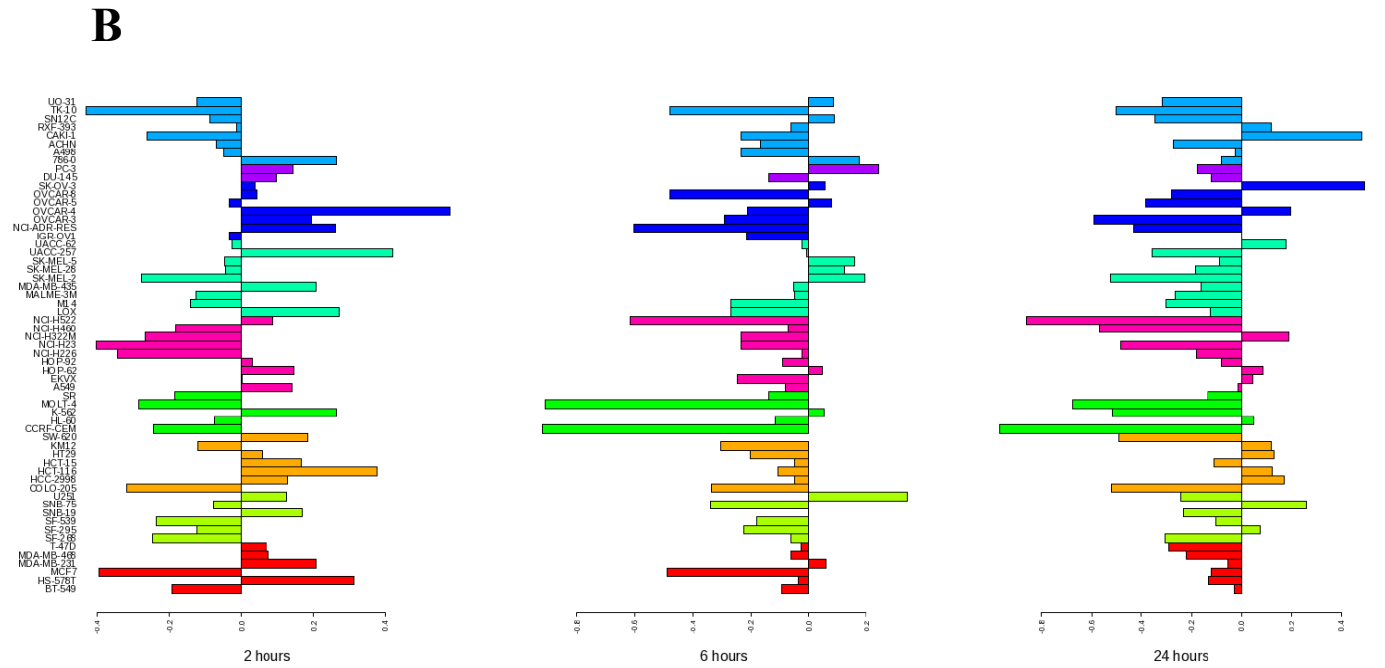
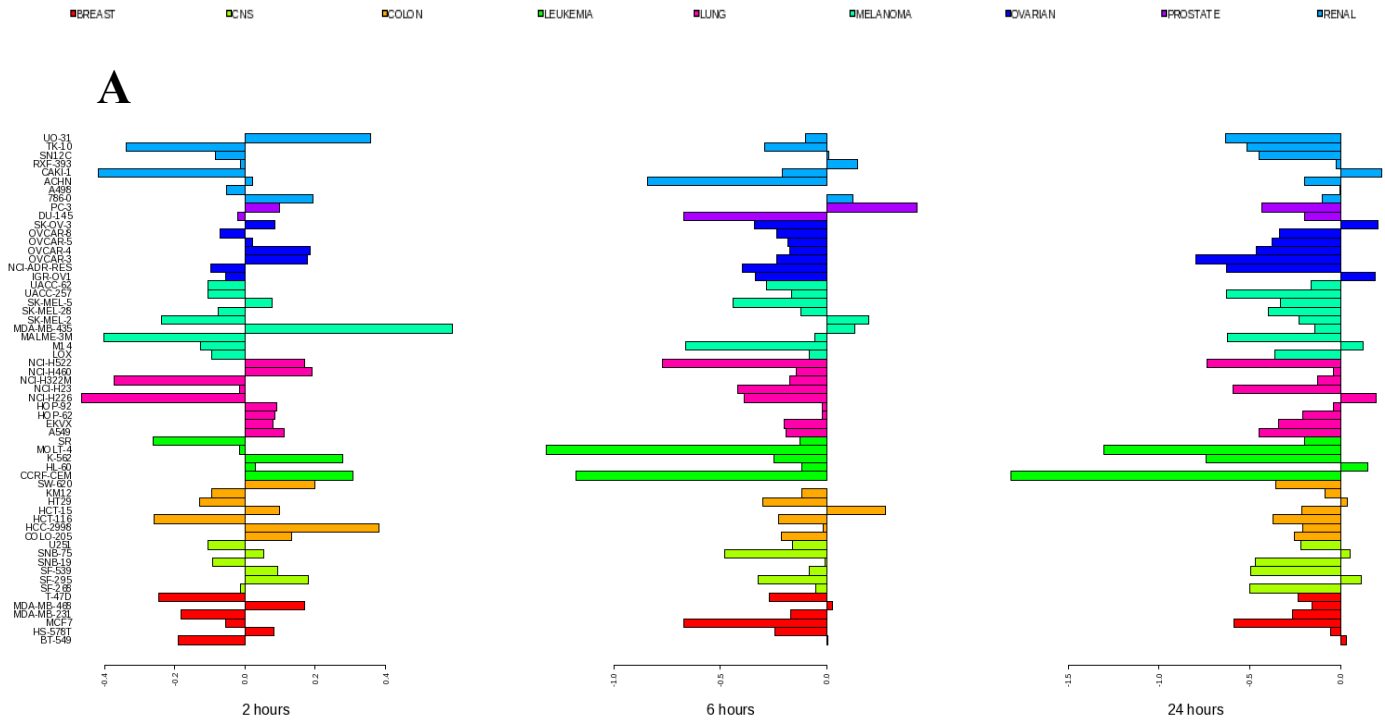
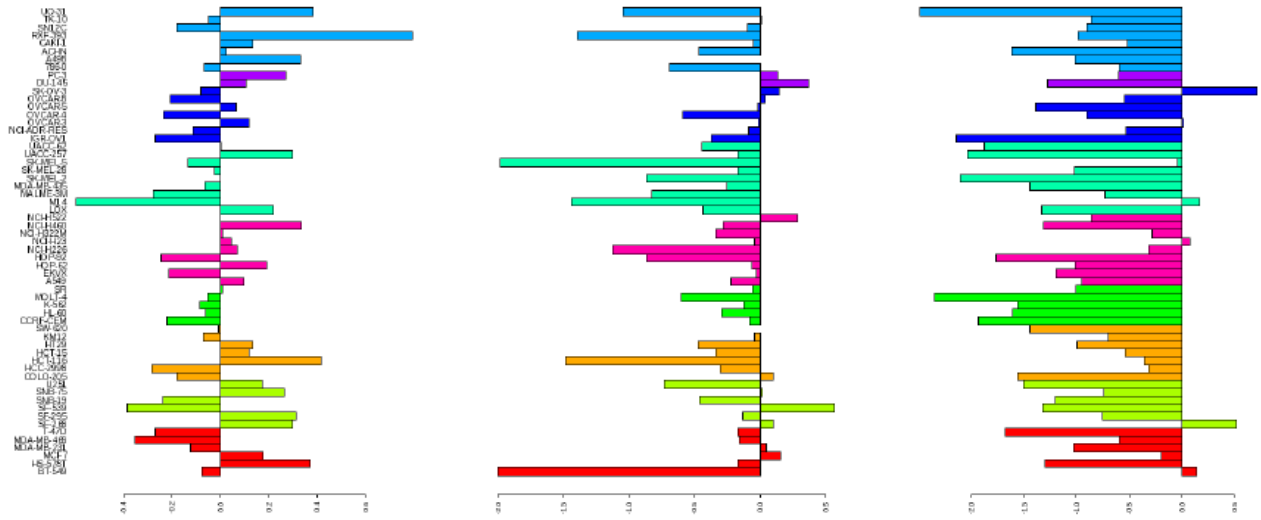


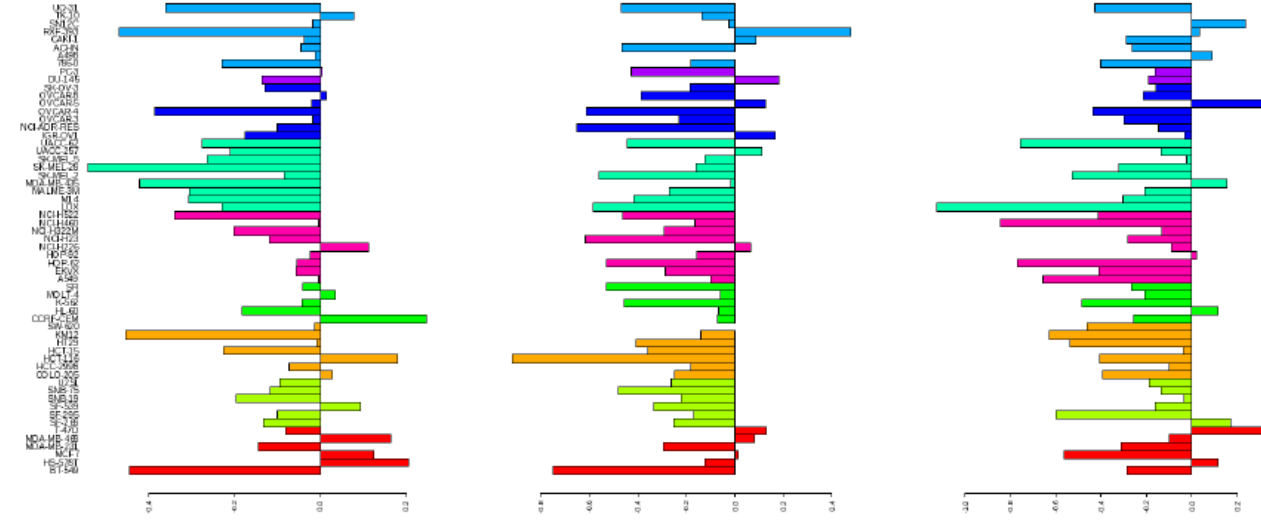
Fig. S10

■ BREAST ■ CNS ■ COLON ■ LEUKEMIA ■ LUNG ■ MELANOMA ■ OVARIAN ■ PROSTATE ■ RENAL

APOBEC3C



TDG



MBD1

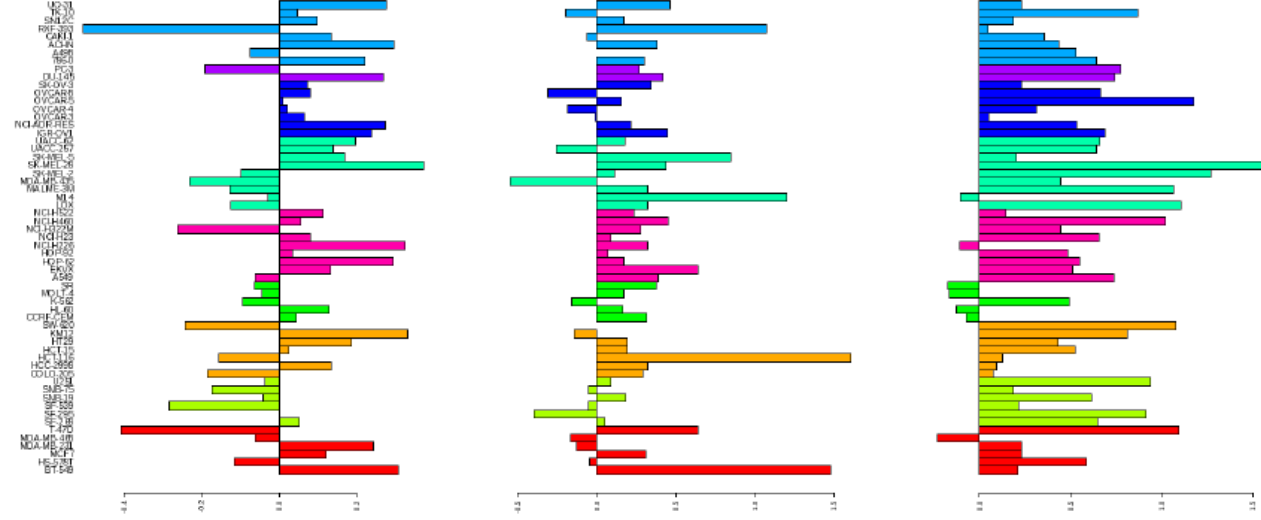


Fig. S11

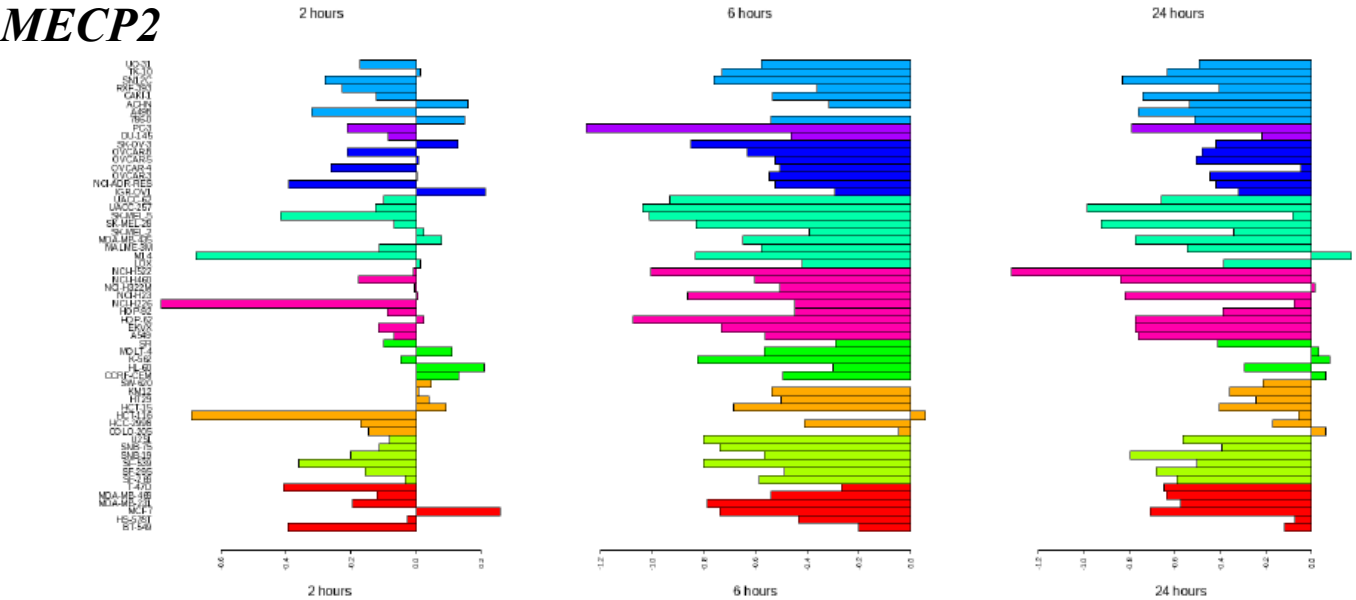
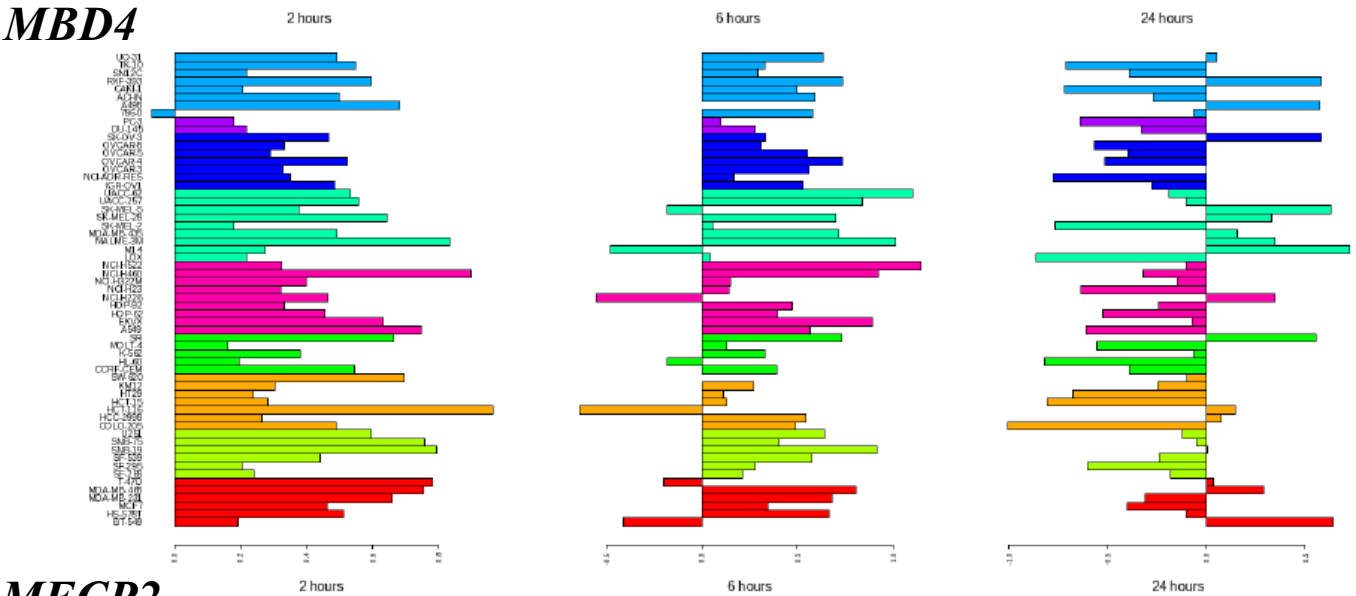
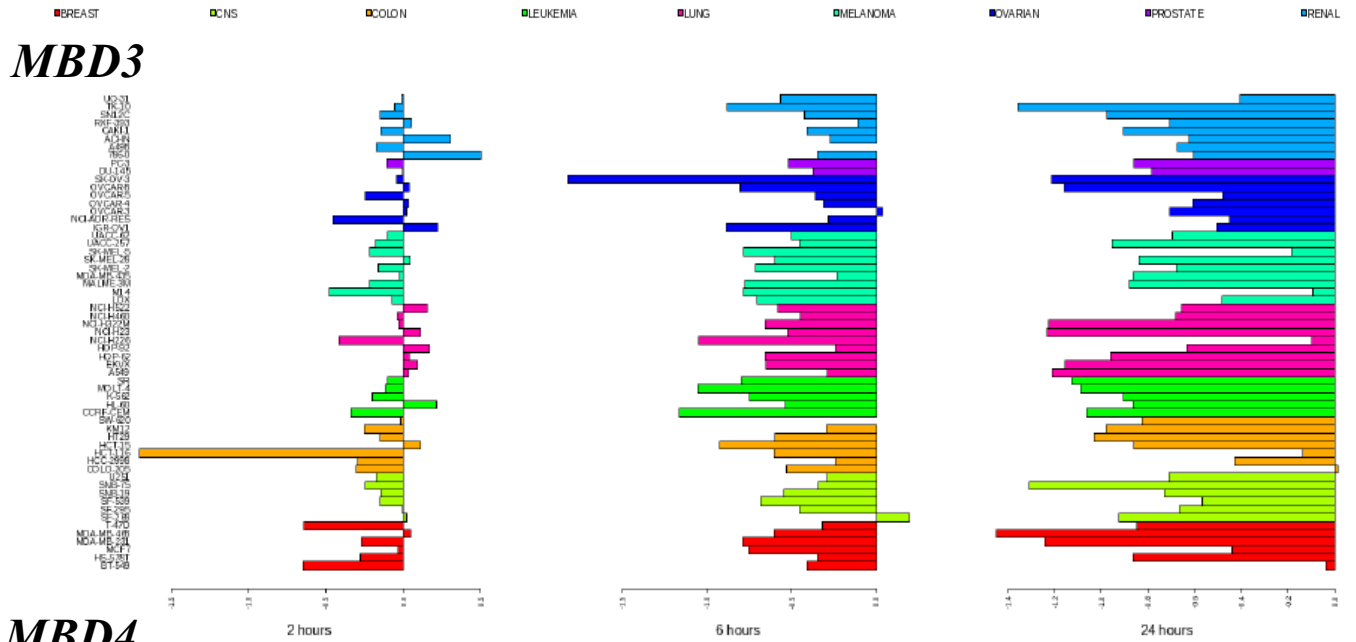
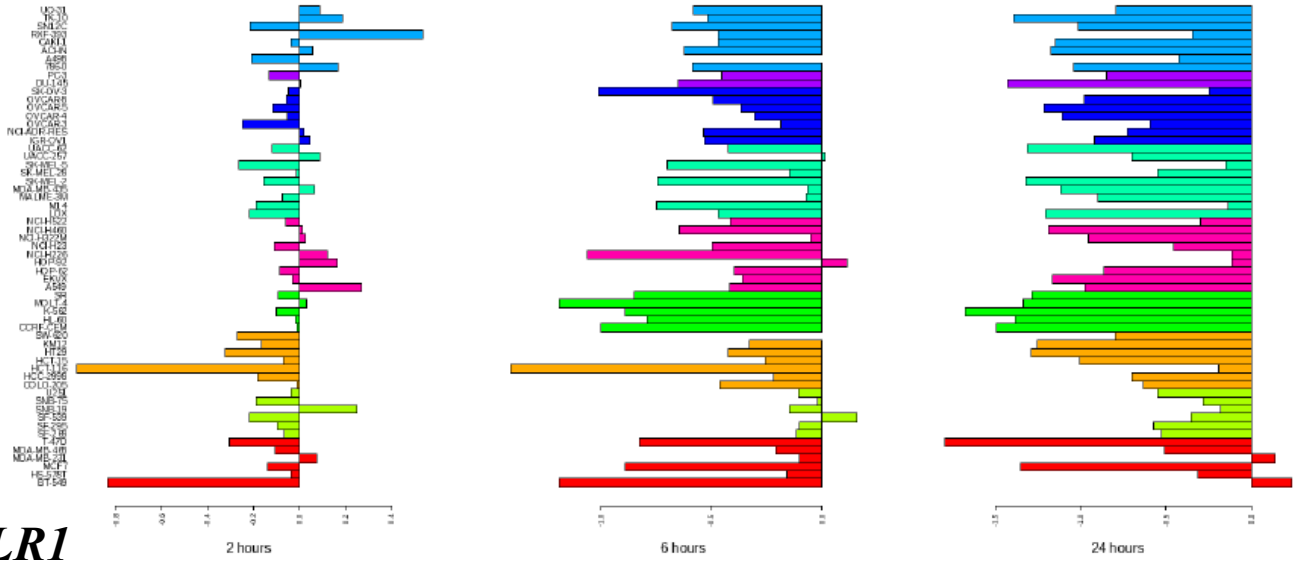


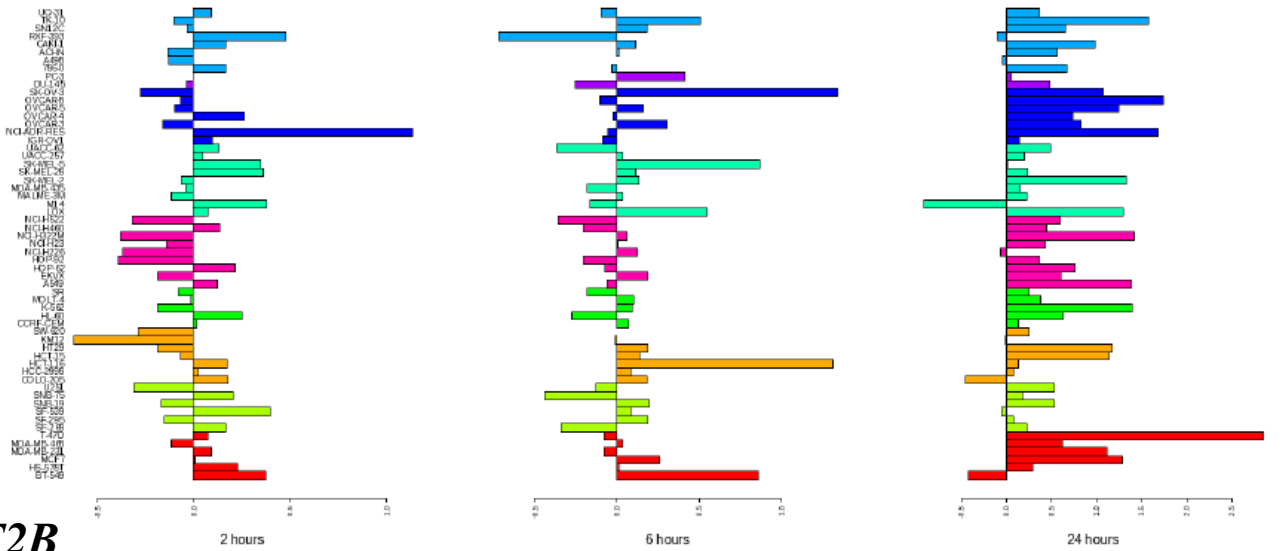
Fig. S11 (cont.)

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SLC19A1



FOLR1



MAT2B

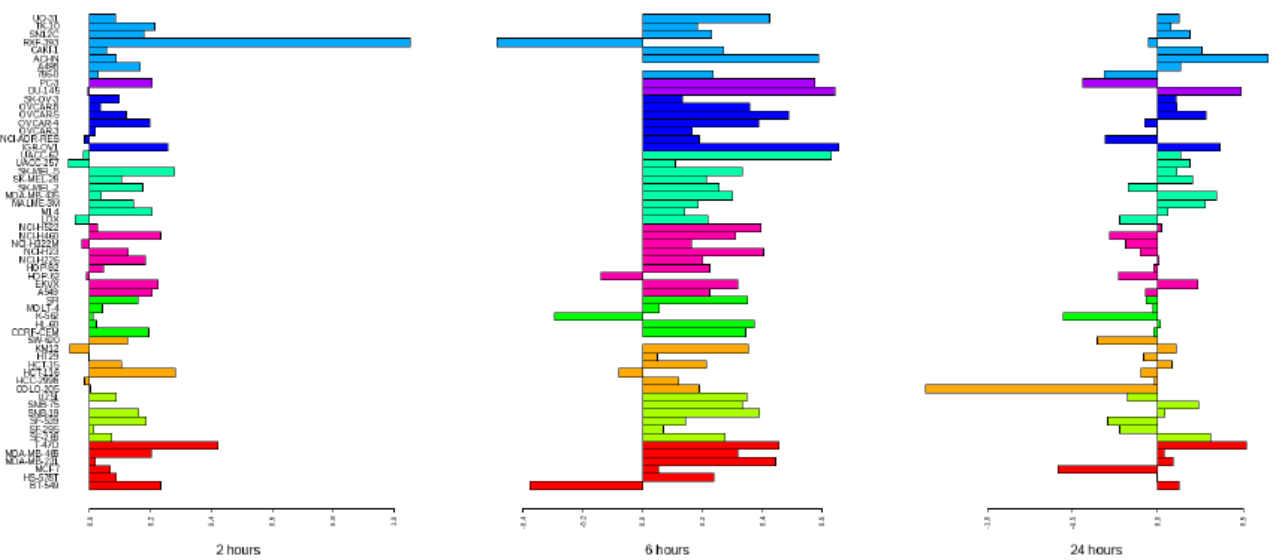


Fig. S12

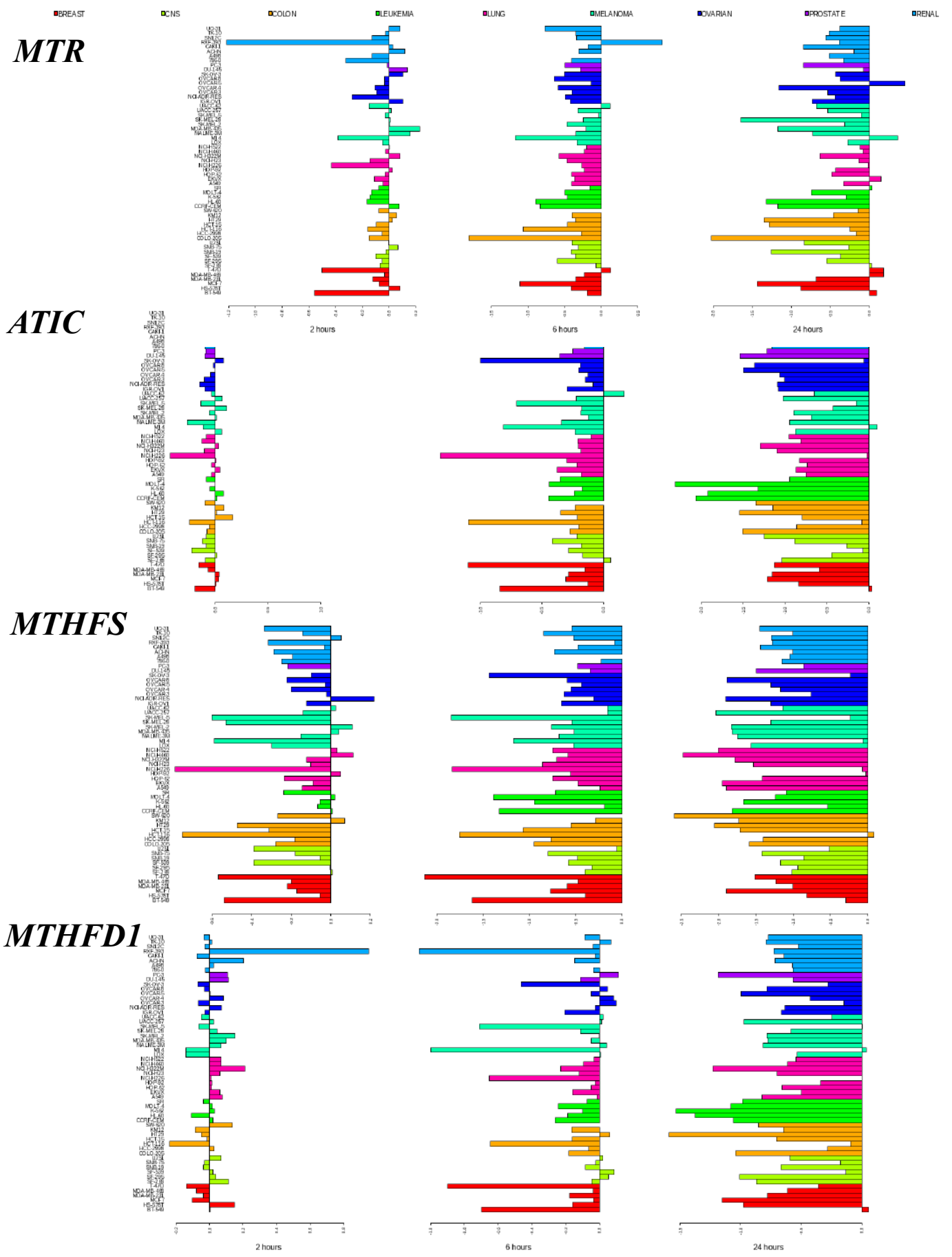


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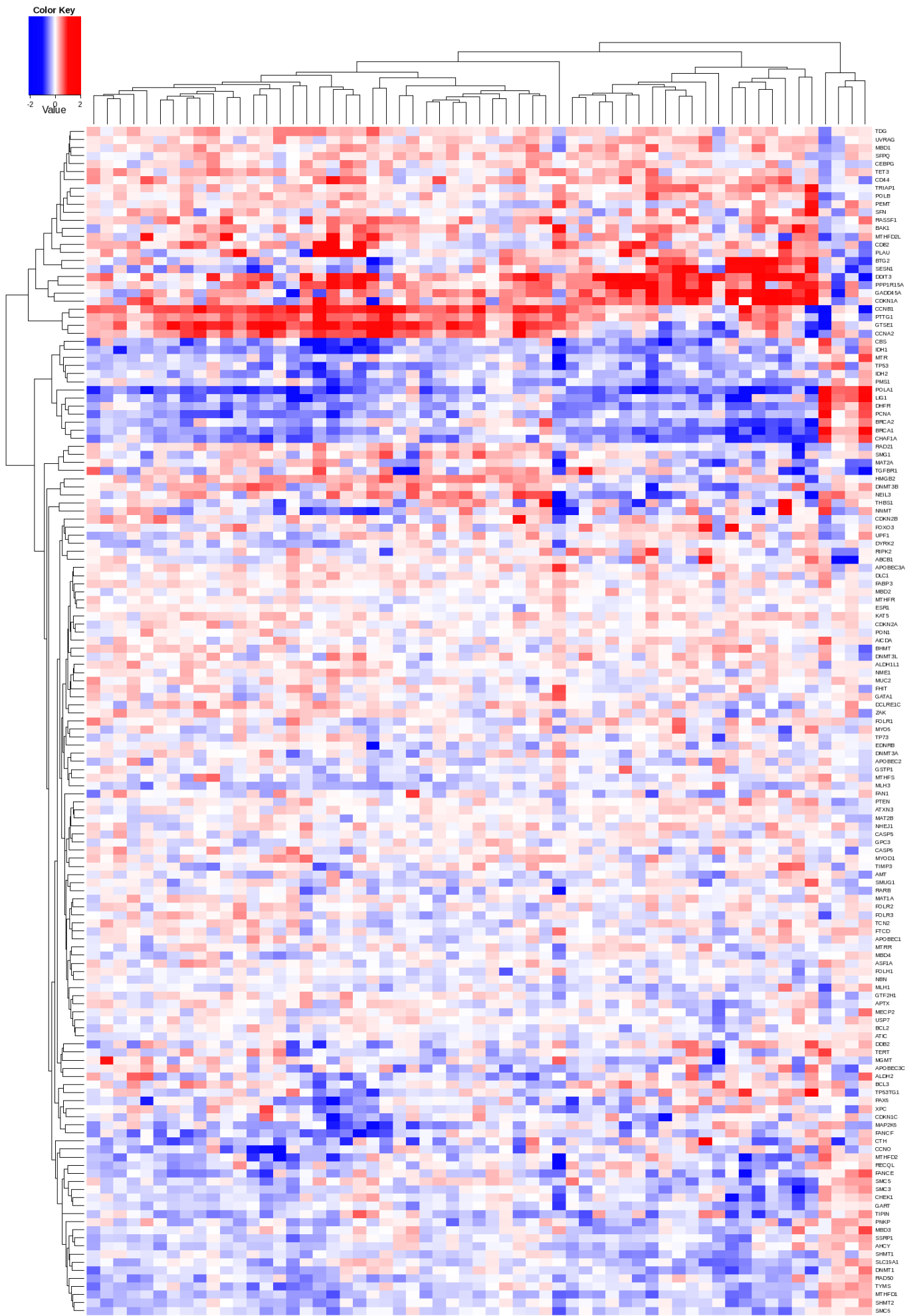


Fig. S13

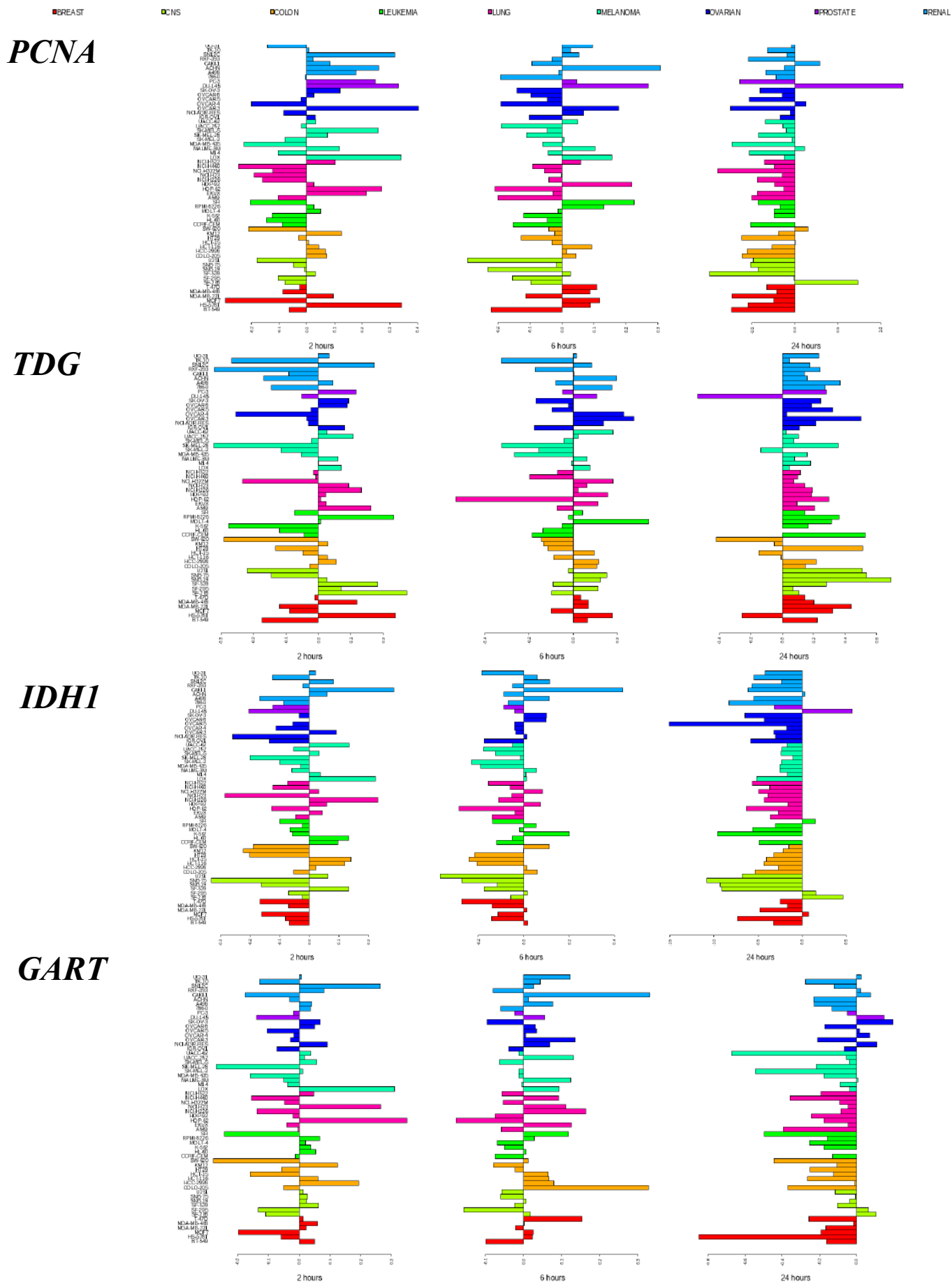


Fig. S14

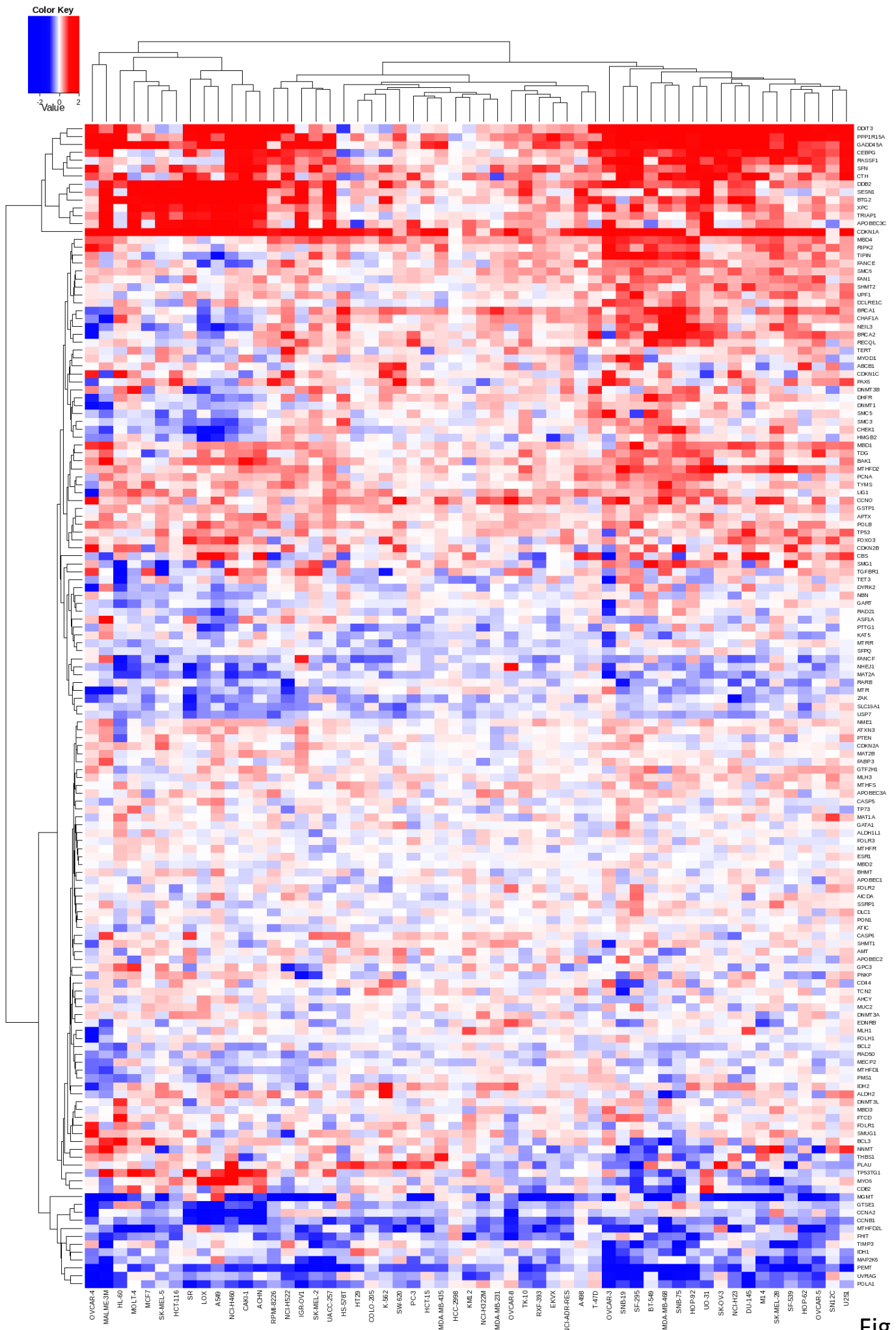
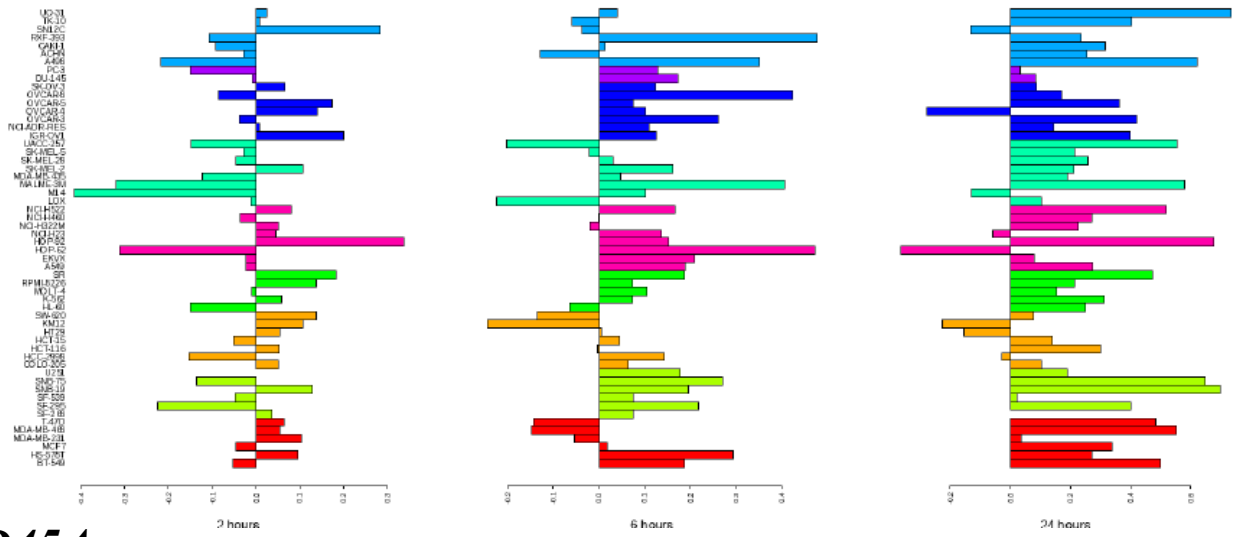


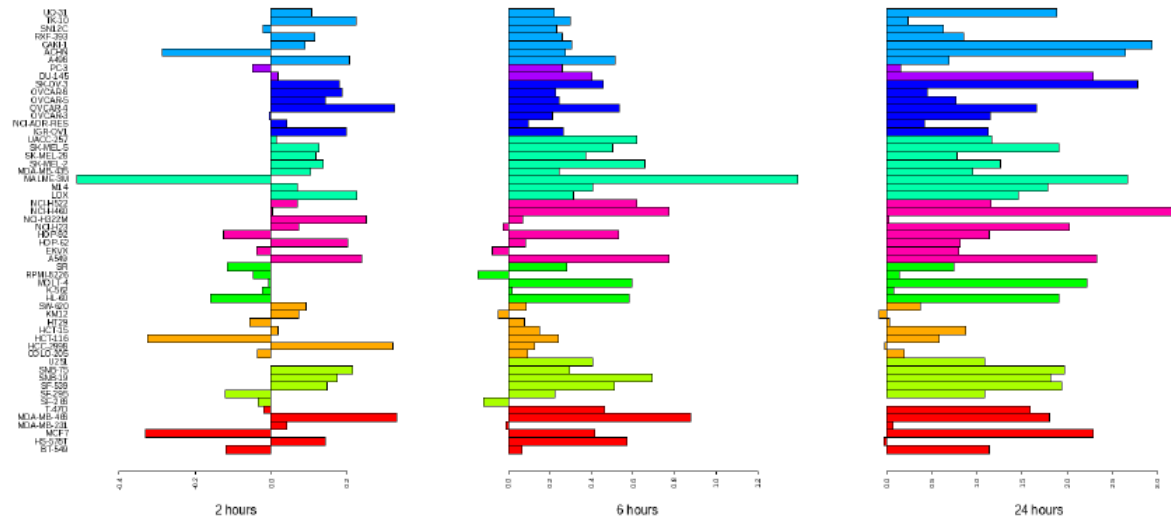
Fig. S15

■ BREAST ■ CNS ■ COLON ■ LEUKEMIA ■ LUNG ■ MELANOMA ■ OVARIAN ■ PROSTATE ■ RENAL

PCNA



GADD45A



MGMT

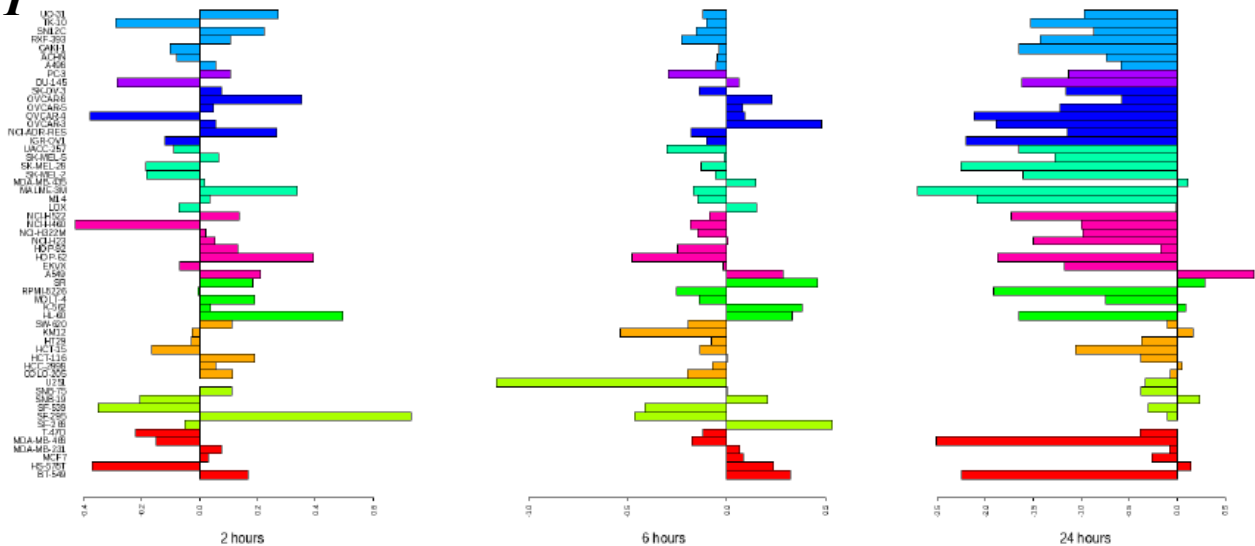
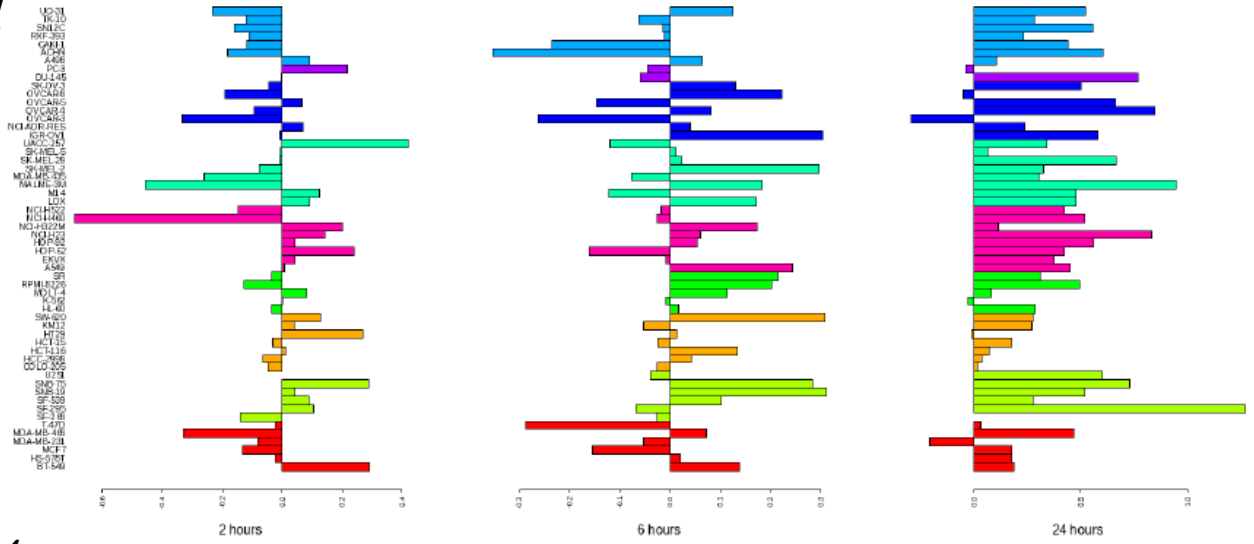


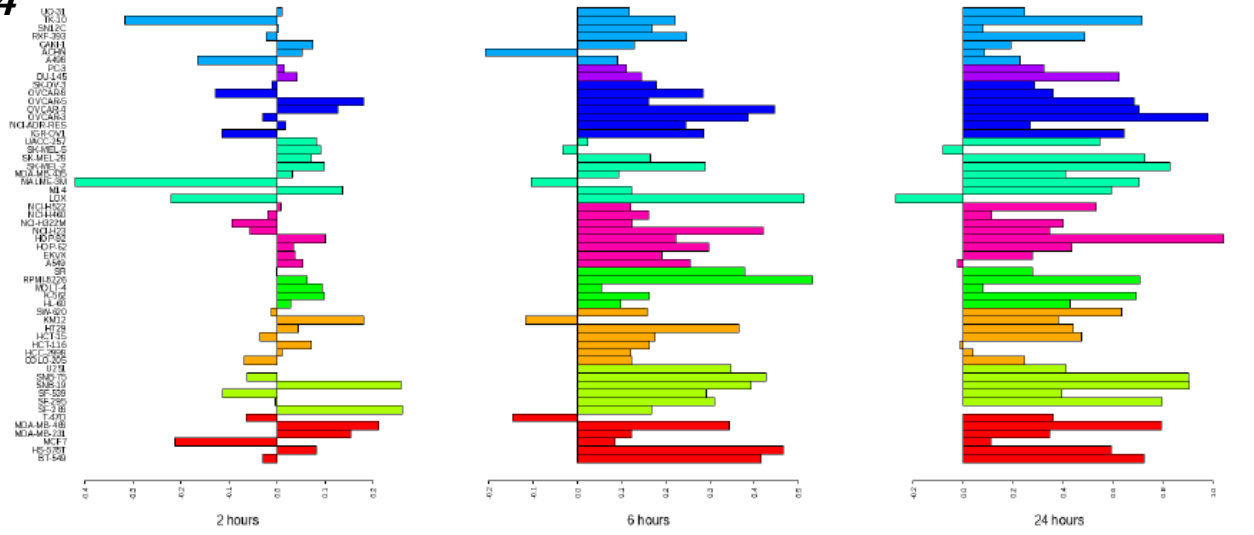
Fig. S16

■ BREAST
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MBD1



MBD4



USP7

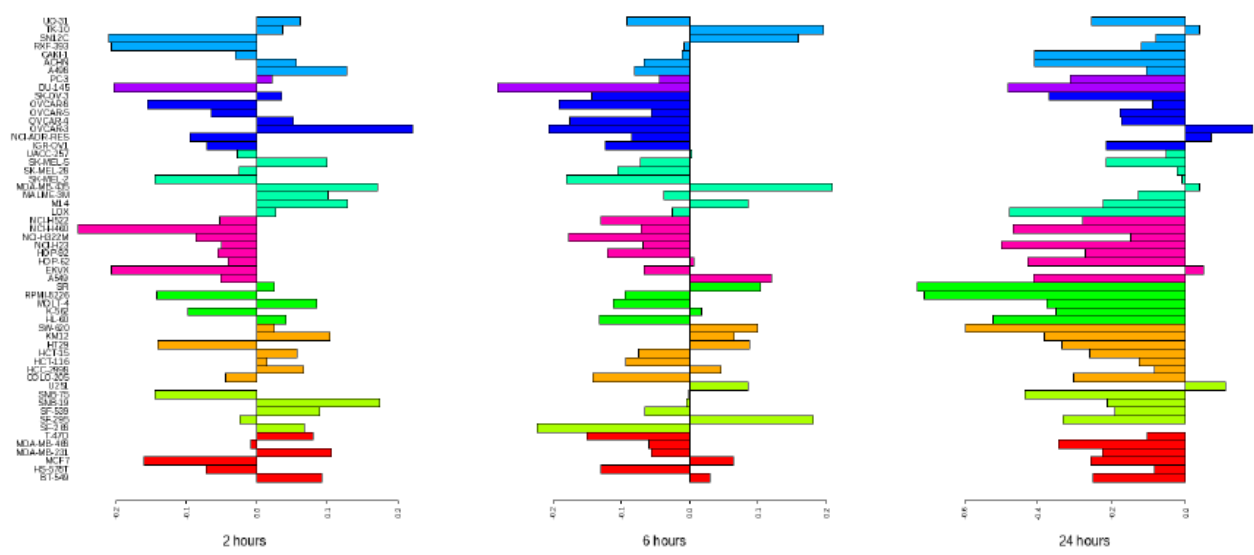
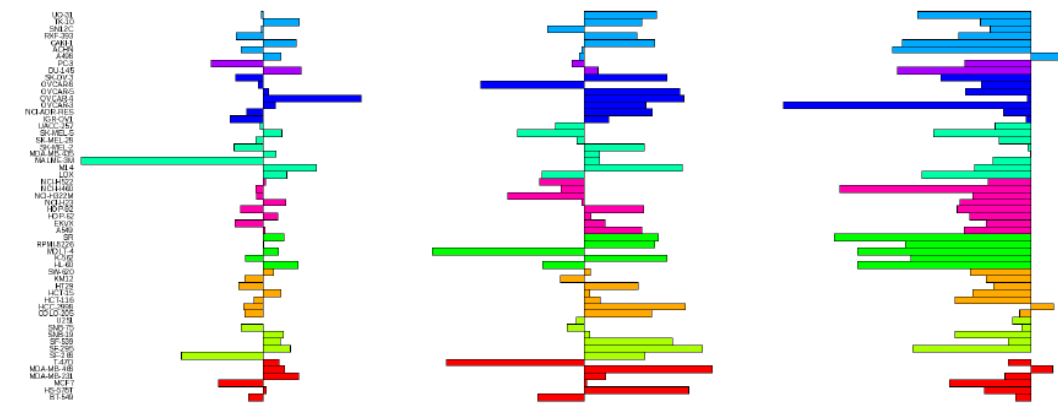
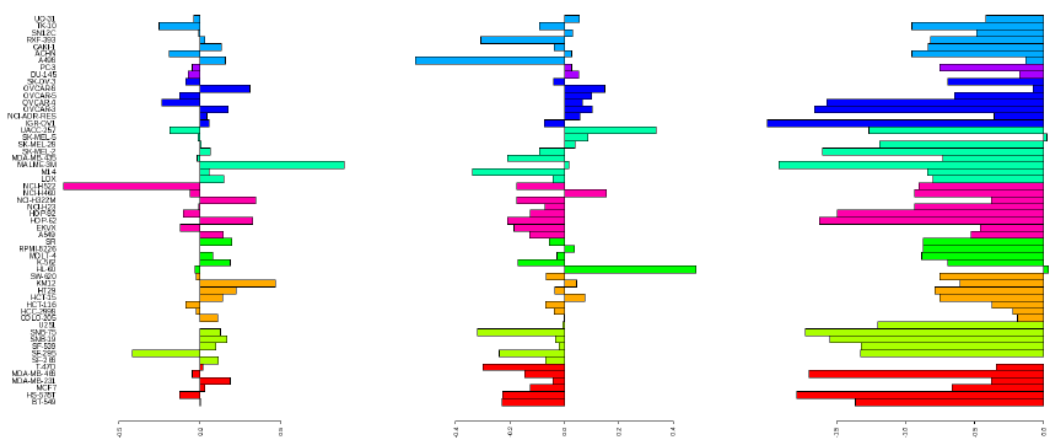


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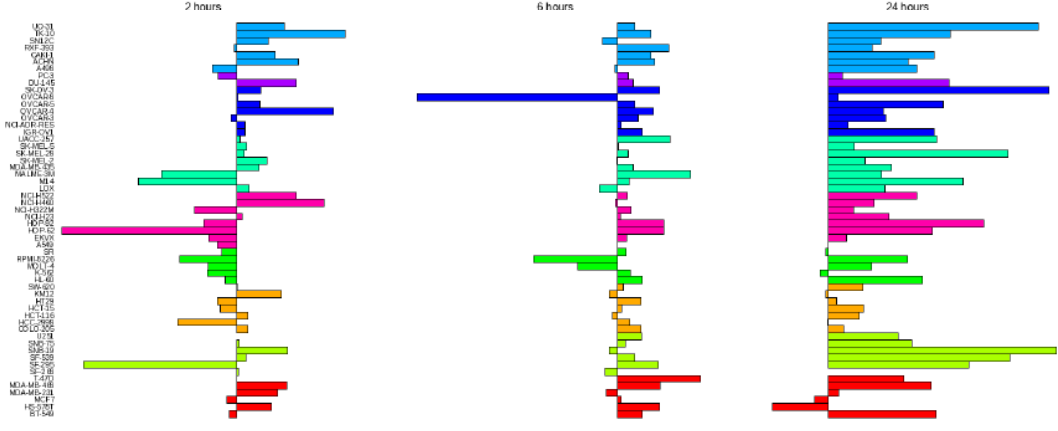
MAT2A



PEMT



MTHFD2



MTHFD2L

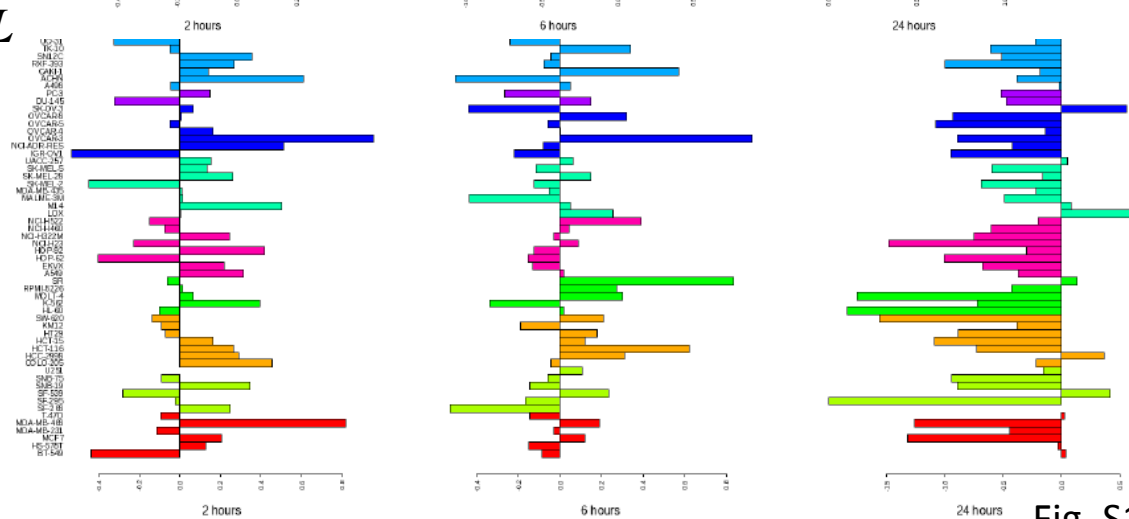


Fig. S17