Supplemental File 2

for

Identification of Novel Activators of the Metal Responsive Transcription Factor (MTF-1) Using a Gene Expression Biomarker in a Microarray Compendium

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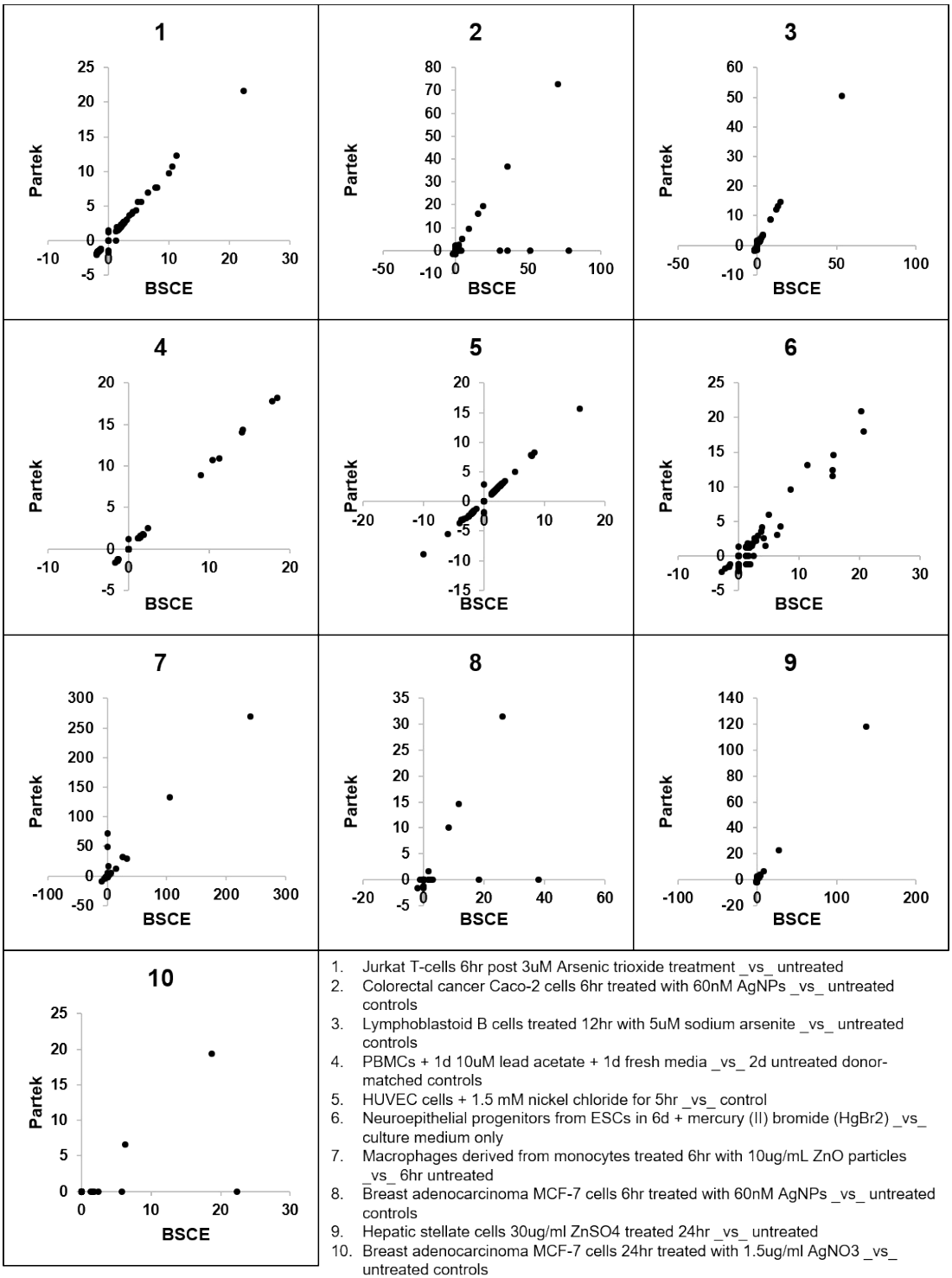

1. Jurkat T-cells 6hr post 3uM Arsenic trioxide treatment _vs_ untreated
2. Colorectal cancer Caco-2 cells 6hr treated with 60nM AgNPs _vs_ untreated controls
3. Lymphoblastoid B cells treated 12hr with 5uM sodium arsenite _vs_ untreated controls
4. PBMCs + 1d 10uM lead acetate + 1d fresh media _vs_ 2d untreated donor-matched controls
5. HUVEC cells + 1.5 mM nickel chloride for 5hr _vs_ control
6. Neuroepithelial progenitors from ESCs in 6d + mercury (II) bromide (HgBr2) _vs_ culture medium only
7. Macrophages derived from monocytes treated 6hr with 10ug/mL ZnO particles _vs_ 6hr untreated
8. Breast adenocarcinoma MCF-7 cells 6hr treated with 60nM AgNPs _vs_ untreated controls
9. Hepatic stellate cells 30ug/ml ZnSO4 treated 24hr _vs_ untreated
10. Breast adenocarcinoma MCF-7 cells 24hr treated with 1.5ug/ml AgNO3 _vs_ untreated controls

Figure S1. Comparison of gene lists from BSCE and those generated in Partek Genomics Suite for the ten biosets used in the biomarker.

Only genes which are present in the biomarker are shown. A minor number of the genes present in BSCE gene lists were found to be insignificant using the Partek method indicating that the

statistical filters used in the Partek analysis were slightly more stringent than those used by BSCE.

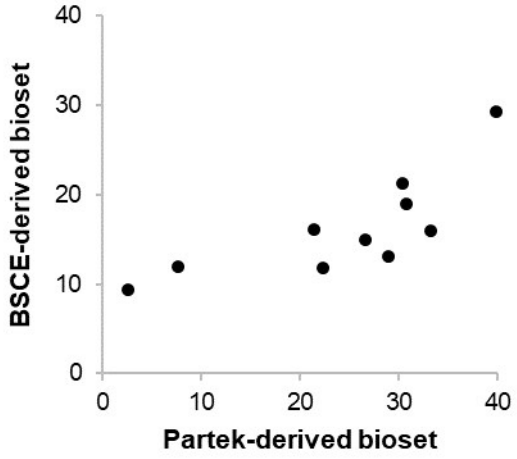

Figure S2. **Comparison of the -log(*p*-value)s from the Partek-derived vs. the BSCE-derived lists.**

A regression analysis indicated an R^2 value of 0.600 (*p*-value = 0.0085) indicating that the biomarker correlations were similar independent of the method used to derive the bioset.

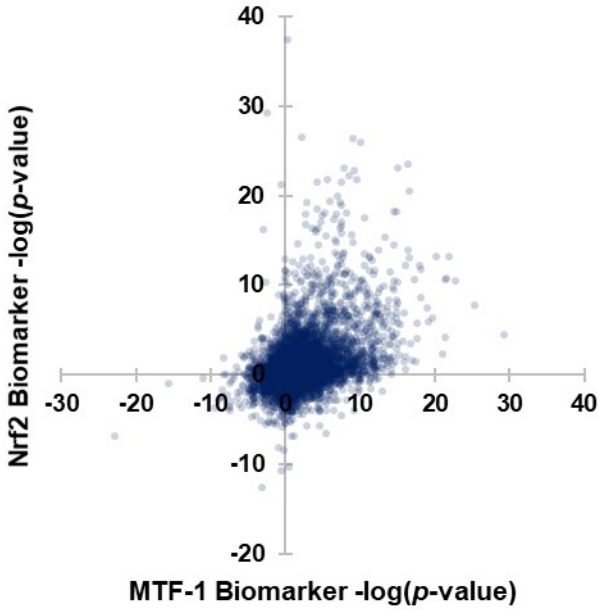

Figure S3. MTF-1 and Nrf2 are simultaneously activated by chemical exposure.

The -log(*p*-value)s for correlations of 11,735 biosets of chemical vs. control comparisons between the Nrf2 and MTF-1 biomarkers are shown.

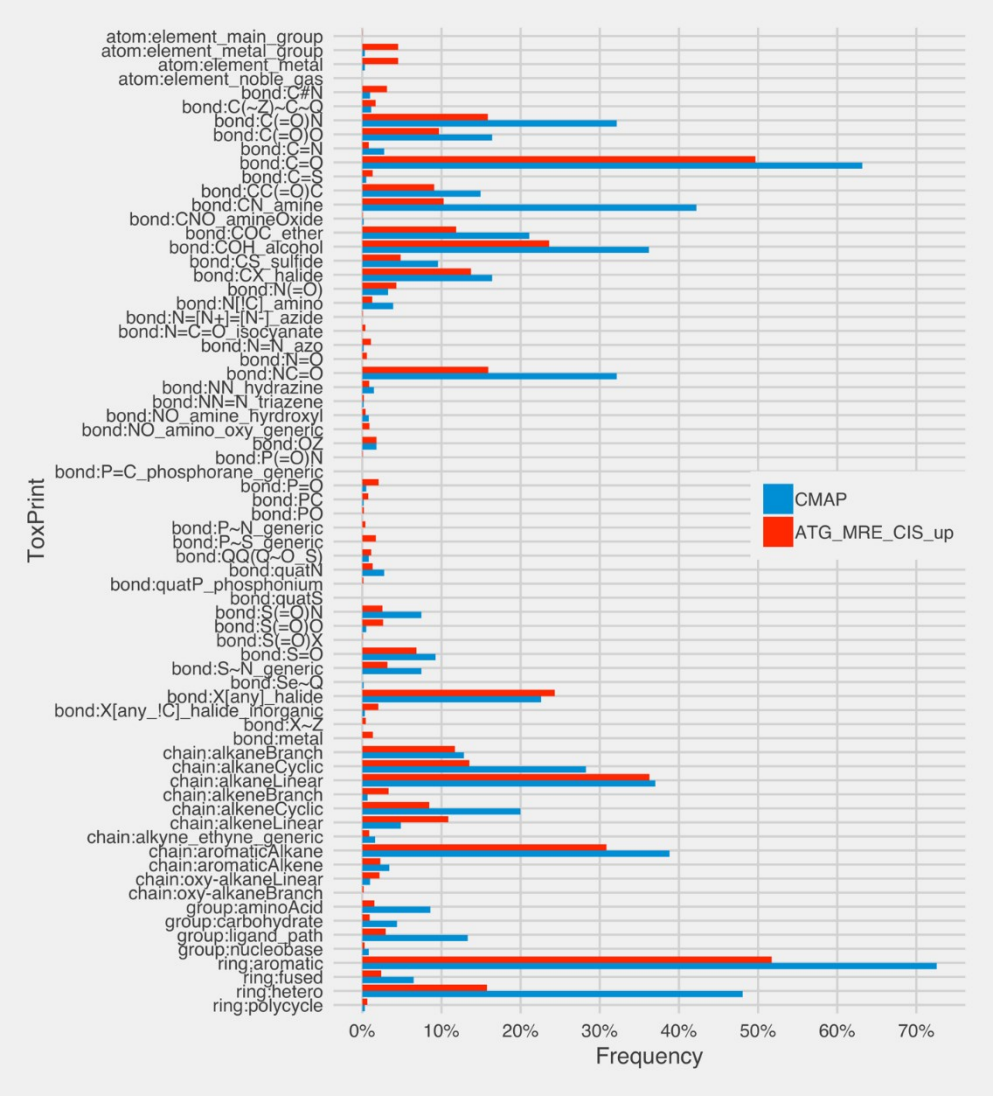

Figure S4. Comparison of the frequency of the 70 "level 2" ToxPrints for the chemicals in the CMAP dataset (blue) and the chemicals tested in the ToxCast ATG_MRE_CIS_up assay (red).

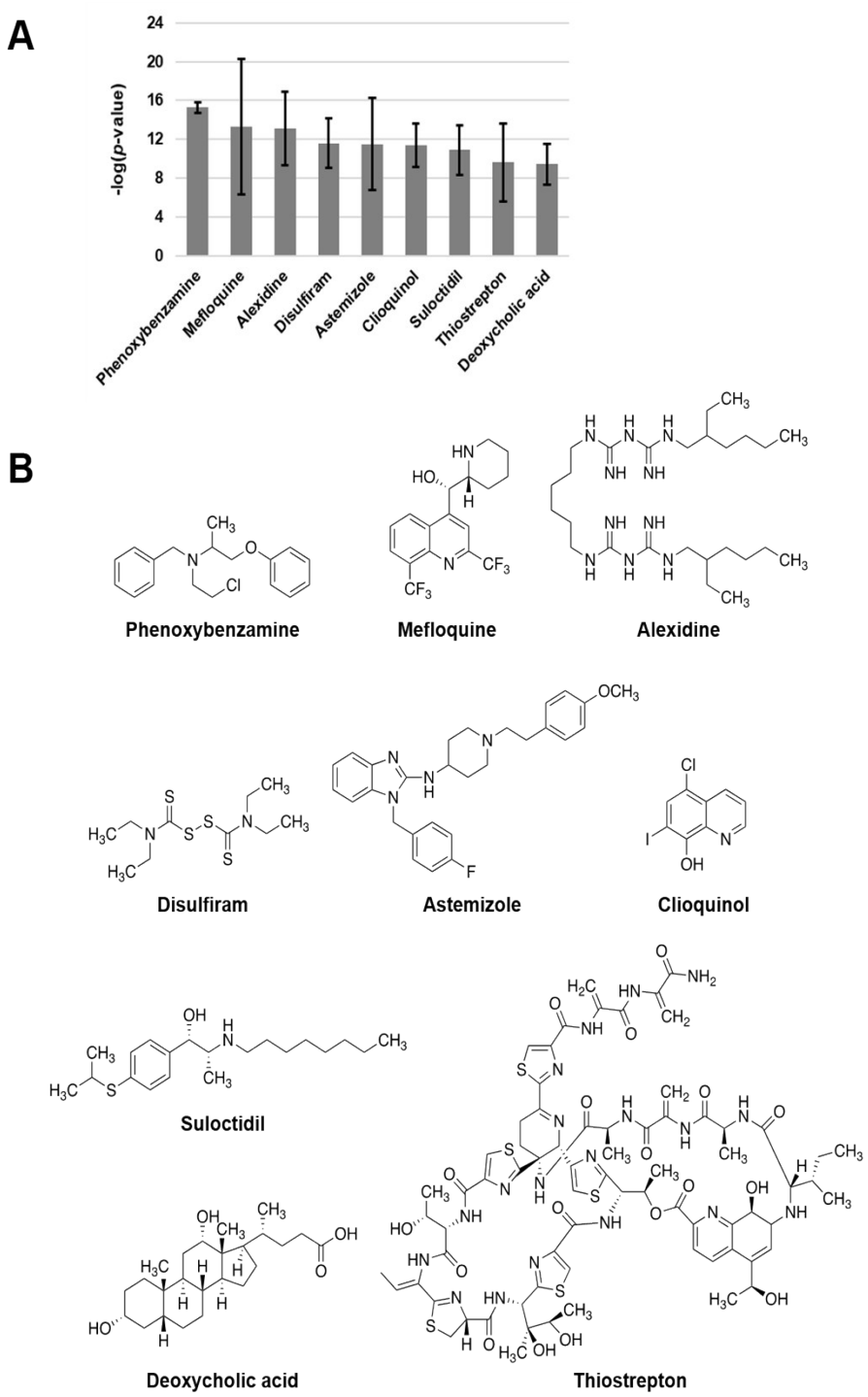

Figure S5. Analysis of nine putative MTF-1 activators.

A. Average -log(*p*-value) of the correlation across biosets for each chemical examined and the MTF-1 biomarker for 9 predicted MTF-1 activators. Error bars show standard deviation (n = 2–4.)

B. Structures of the nine chemicals.

Figure S6. Identification of genes that exhibit expression changes in the MTF-1-null cells.

Control wild-type MCF-7 and control MTF-1-null cells were examined for expression changes using TempO-Seq human 1500+ platform examining the expression changes in ~3000 genes. Significant expression differences between *MTF1*-null vs. wild-type cells were identified as described in the Methods. There were 44 genes that were differentially expressed in the *MTF1*-null vs. wild-type comparison.