Molecular characterization of breast cancer cell response to metabolic drugs

SUPPLEMENTARY MATERIALS

Supplementary Table 1: SNP array. See Supplementary_Table_1

Supplementary Table 2: Protein data. See Supplementary_Table_2

Supplementary Table 3: MTF delta values. See Supplementary_Table_3

Supplementary Table 4: RP delta values. See Supplementary_Table_4

Supplementary Table 5: Prediction of MTF response using proteomics data

Protein	B	Std. error	Beta	Sig
MMGT1	120.295	0.342	1.070	0.000
IDH1	8.233	0.118	0.208	0.000
PSPC1	2.559	0.109	0.068	0.000
TACO1	−1.279	0.129	-0.033	0.000

Linear regression model that predicts MTF response (adjusted $R^2 = 1$) using protein expression data. B = constant, Std. error = standard error, Beta = covariate, Sig = statistical significance.

Supplementary Table 6: Prediction of RP response using proteomics data

Protein	B	Std. error	Beta	Sig
ACADSB	−14.894	0.154	−0.838	0.000
CCDC58	7.248	0.208	0.330	0.000
MPZL1	−1.837	0.105	−0.094	0.000
SBSN	−1.945	0.307	−0.079	0.000

Linear regression model that predicts RP treatment response (adjusted $R^2 = 1$) using proteomics data. B = constant, Std. error = standard error, Beta = covariate, Sig = statistical significance.

Supplementary Table 7: Prediction of RP response using functional data

Model	B	Std. error	Beta	Sig
Constant	1.095	0.075		0.001
Metabolism A	−2.171	0.282	−0.960	0.005
Metabolism B	−1.149	0.356	−0.403	0.048

Multiple linear regression model predicting response against RP treatment. B = constant, Std. error = standard error, Beta = covariate, Sig = statistical significance.

Supplementary Table 8: Cytometry experiments. See Supplementary_Table_8

Supplementary Table 9: FBA and FVA results. See Supplementary_Table_9

Supplementary Table 10: Prediction of MTF response using flux data

Model	B	Std. error	Beta	Sig
Constant	0.779	0.002		
Glutamate metabolism	−2.379	0.016	−0.848	0.004
Pyruvate metabolism	0.083	0.002	0.224	0.016

Linear regression model using flux activities to predict MTF response. B = constant, Std. error = standard error, Beta = covariate, Sig = statistical significance.

Supplementary Table 11: Prediction of RP response using flux data

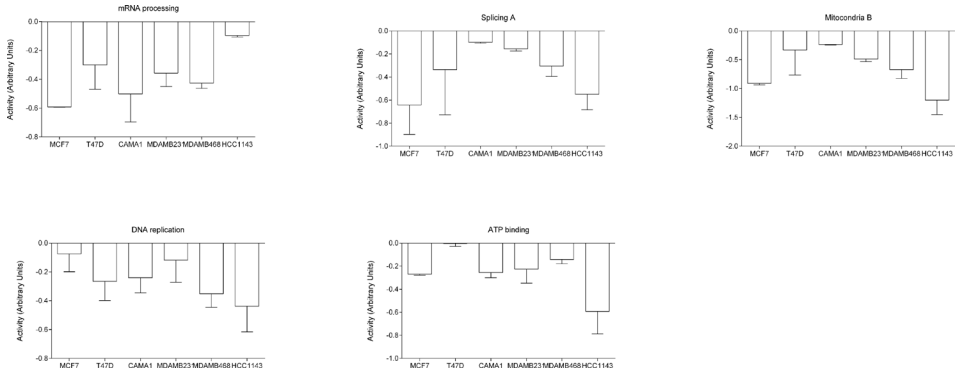
Model	B	Std. error	Beta	Sig
Constant	0.761	0.001		0.000
Valine, leucine and isoleucine metabolism	2.018	0.002	0.929	0.001
Cholesterol metabolism	0.045	0.000	0.093	0.007

Linear regression model using flux activities to predict RP response. B = constant, Std. error = standard error, Beta = covariate, Sig = statistical significance.

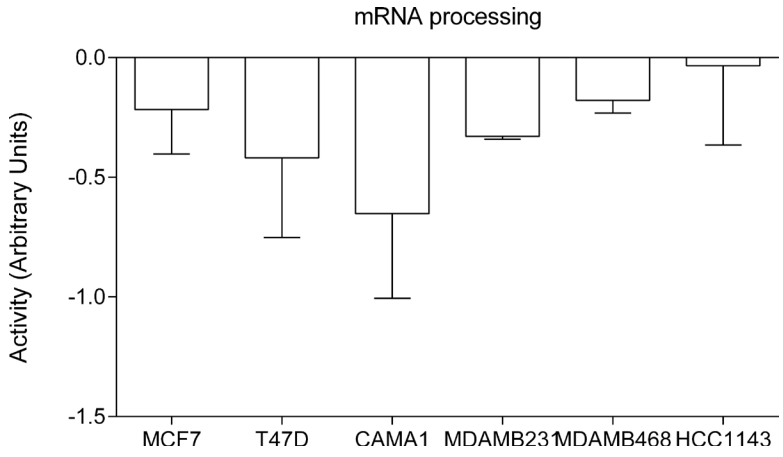
Supplementary Table 12: Catalase and superoxide dismutase delta values between control and MTF-treated cell lines

Cell line	Catalase	Superoxide dismutase
MCF7	0.36	0.31
T47D	0.18	1.3
CAMA1	−0.15	1.25
MDAMB231	0.11	0.45
MDAMB468	0.20	0.09
HCC1143	0.39	0.90

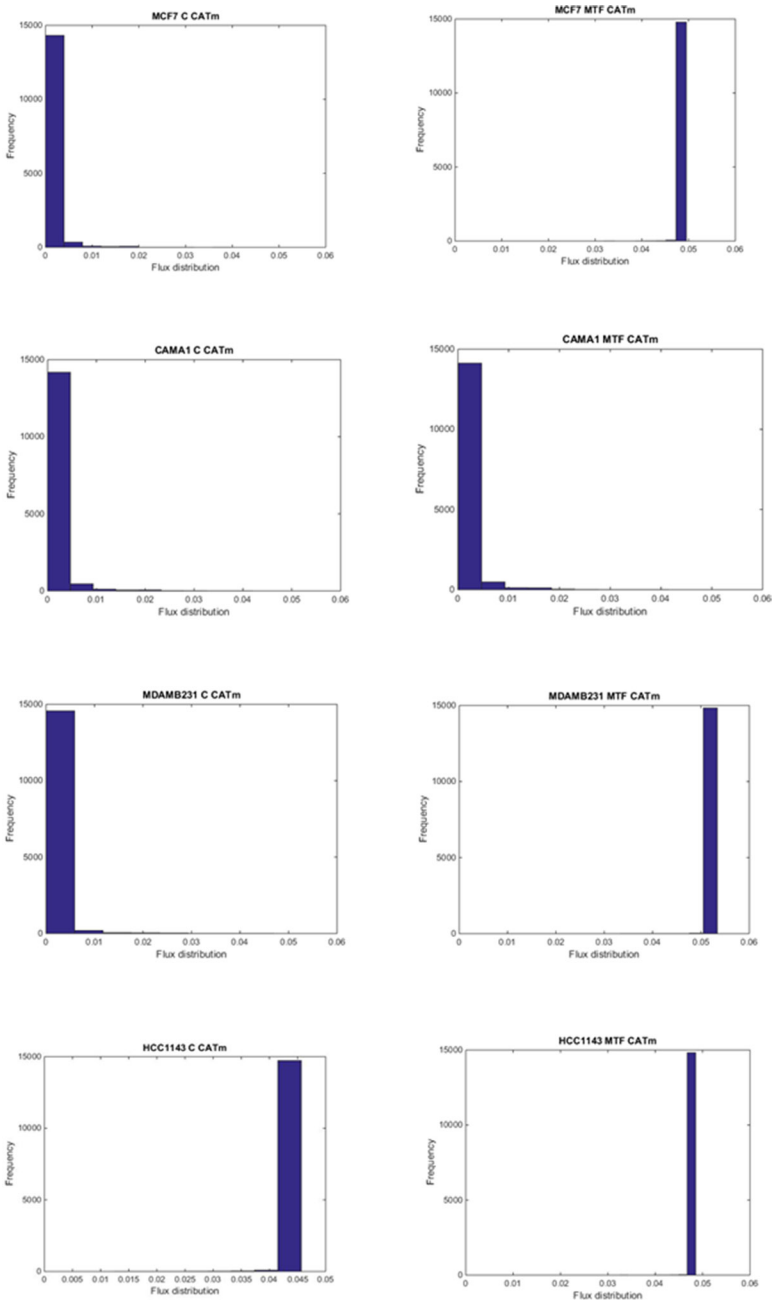
Delta was calculated, subtracting MTF catalase and superoxide dismutase cell fluxes to control cell fluxes.



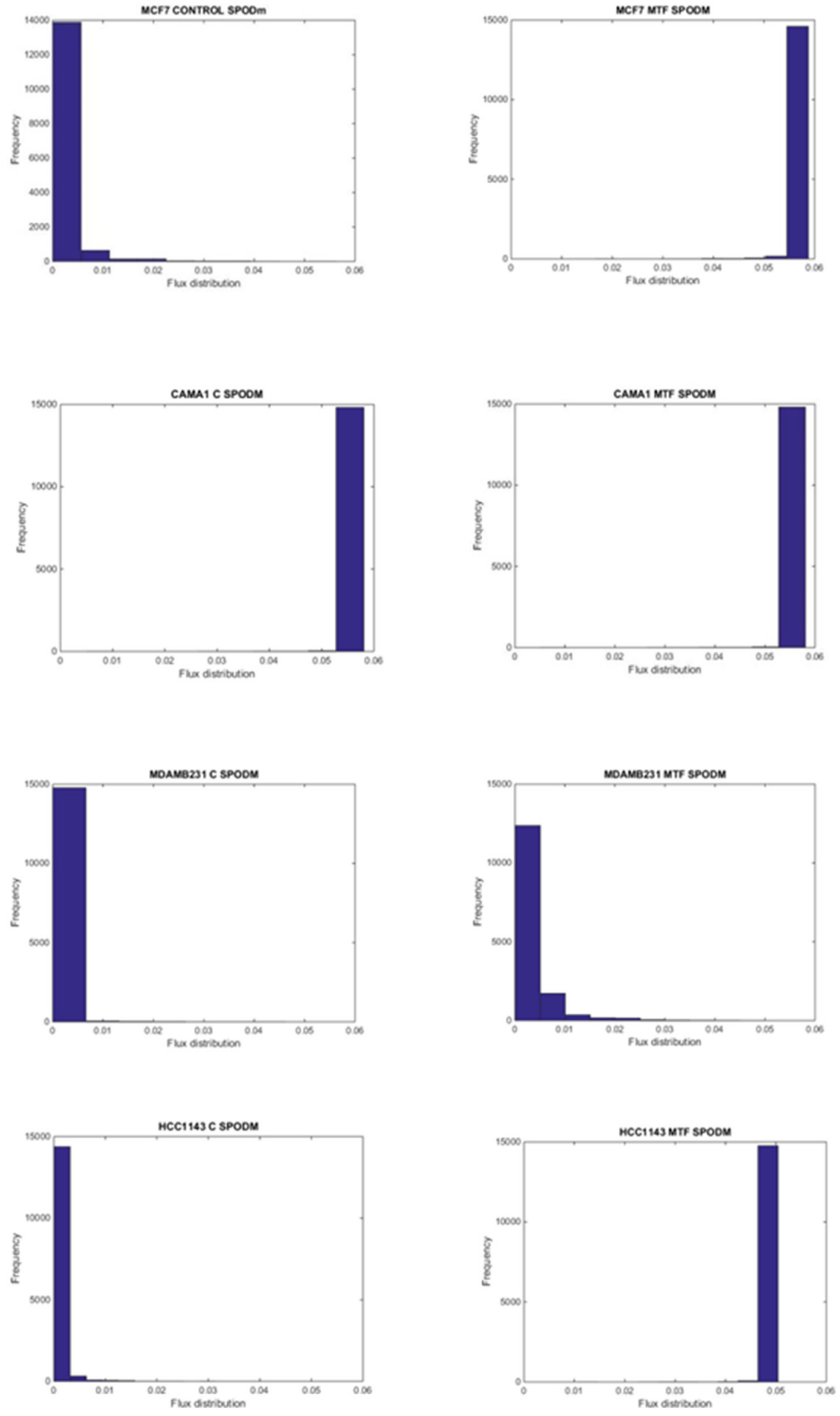
Supplementary Figure 1: Node activity measurements for cell lines treated with MTF with a decrease in functional node activity in all cell lines.



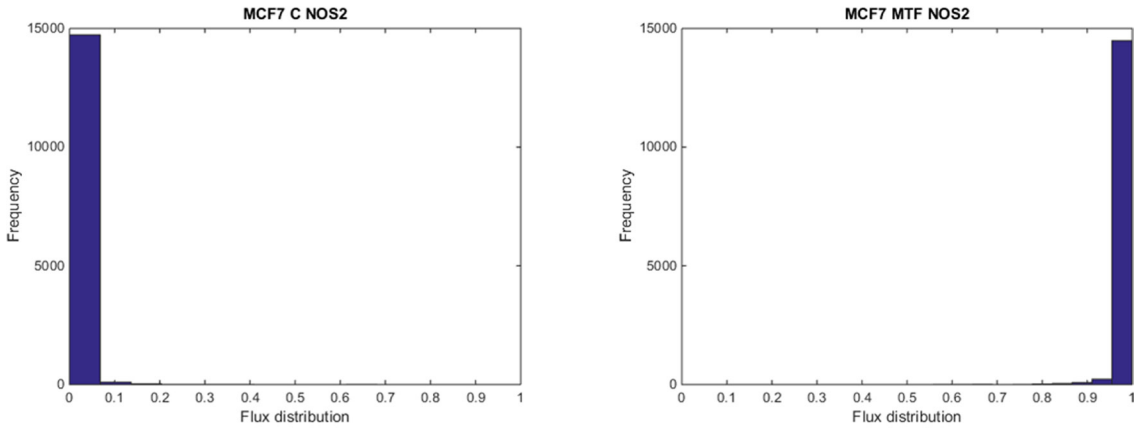
Supplementary Figure 2: Node activity measurements for cell lines treated with RP with a decrease in functional node activity in all cell lines.



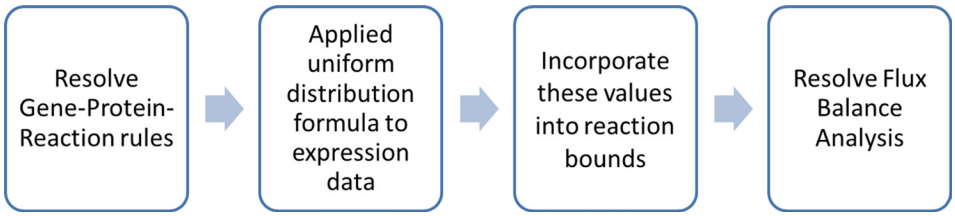
Supplementary Figure 3: Distribution of possible fluxes of catalase (CATm) in control and MTF cell cultures. On the y-axis, frequency is represented; understood as number of possible flux combinations provided by Monte Carlo resampling.



Supplementary Figure 4: Distribution of possible fluxes of superoxide dismutase (SPODM) in control and MTF cell cultures. On the y- axis, frequency is represented; understood as number of possible flux combinations provided by Monte Carlo resampling.



Supplementary Figure 5: Distribution of possible fluxes of nitric oxide synthase (NOS2) in control and MTF MCF7 cell cultures. The model predicts an increase in NO in MTF-treated MCF7 cells regarding the control. On the y- axis, frequency is represented; understood as number of possible flux combinations provided by Monte Carlo resampling.



Supplementary Figure 6: E-flux flowchart.

Supplementary Files 1–12: Monte Carlo sampling for each cell line and condition. (S1 File: MCF7 Control 1, S2 File: MCF7 MTF 1, S3 File: MCF7 RP 1, S4 File: CAMA1 Control 1, S5 File: CAMA1 MTF 1, S6 File: CAMA1 RP 1, S7 File: MDAMB231 Control 1, S8 File: MDAMB231 MTF 1, S9 File: MDAMB231 RP 1, S10 File: HCC1143 Control 1, S11 File: HCC1143 MTF 1, S12 File: HCC1143 RP 1).

Supplementary File 13: Code to incorporate normalized protein expression data into the model. This data needs to be previously normalized using modified E-flux. See Supplementary_File_13