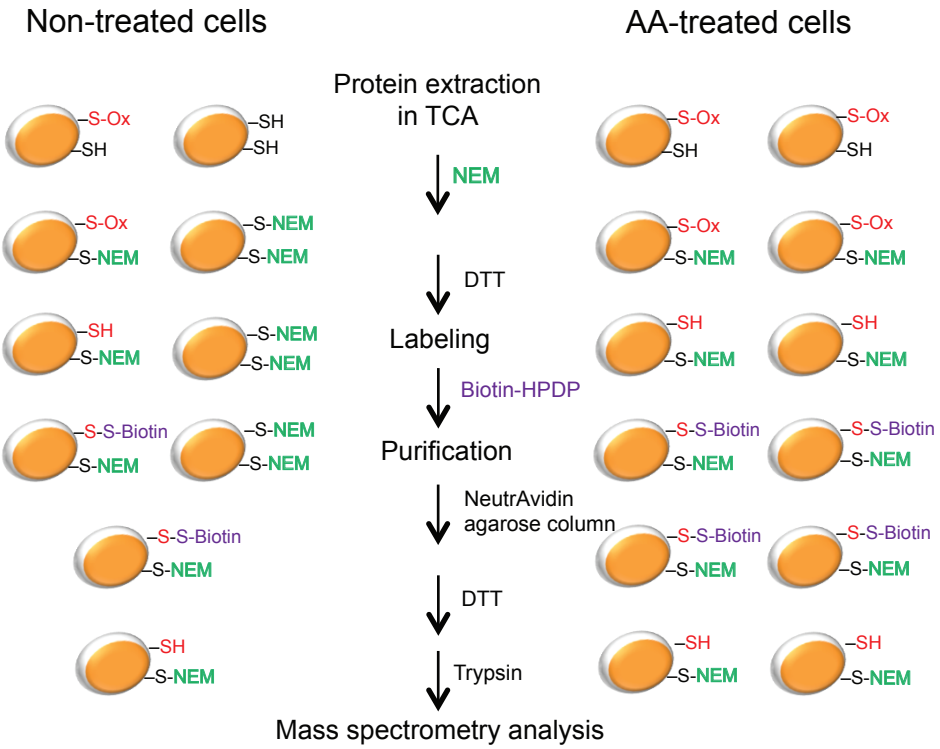


Supplementary Fig.1. Mass spectrometry “redoxome” method to identify the differentially oxidized cysteine-containing proteins upon AA treatment. Details of the protocol and analysis are described in Supplementary Materials and Methods. In short, total proteins from non-treated and 10 mM AA-treated MDA-MB-231 cells for ½ hour were extracted in TCA and resuspended in NEM to protect cysteine-free thiols. Proteins were resuspended in DTT to reduce the oxidized thiols of cysteine-containing proteins. Extracts were resuspended in EZ-Link Biotin-HPDP to allow labeling of newly reduced thiols. For purification of the biotin-tagged proteins, extracts were incubated with NeutrAvidin Agarose Resins and then the biotynilated fraction is eluted with DTT. Oxidized cysteine-containing proteins prepared from cells were digested and analyzed in triplicate with an Orbitrap Fusion Tribrid. Redoxomes from non-treated and AA-treated cells were compared. Proteins with significant variations of protein oxidation (fold change over 1.5 in at least one of the two biological experiments) and associated Anova P value lower than 0.05 between the two conditions were identified.

A

Top Canonical Pathways

Name	*P* value	Overlap	
NRF2-mediated Oxidative Stress Response	2.19E-05	5.0 %	10/199
Aryl Hydrocarbon Receptor Signaling	6.29E-05	5.7 %	8/141
Hepatic Firbosis / Hepatic Stellate Cell Activation	7.91E-05	4.8 %	9/187
Regulation of Cellular Mechanics by Calpain Protease	3.34E-04	7.9 %	5/63
Huntington's Disease Signaling	6.79E-04	3.6%	9/250

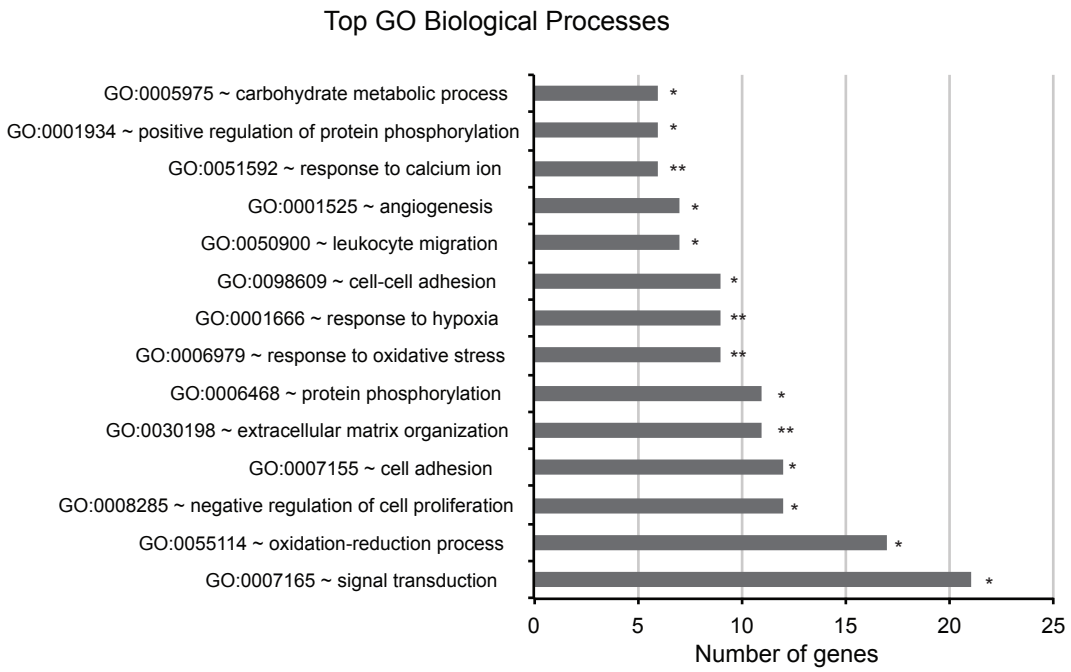
Molecular and Cellular Functions

Name	*P* value	# Molecules
Cellular Movement	1.74E-04 – 1.77E-15	85
Cellular Death and Survival	1.63E-04 – 5.48E-14	98
Cellular Assembly and Organization	1.52E-04 – 9.37E-10	59
Cellular Function and Maintenance	1.53E-04 – 9.37E-10	84
Cellular Development	1.78E-04 – 2.37E-08	91

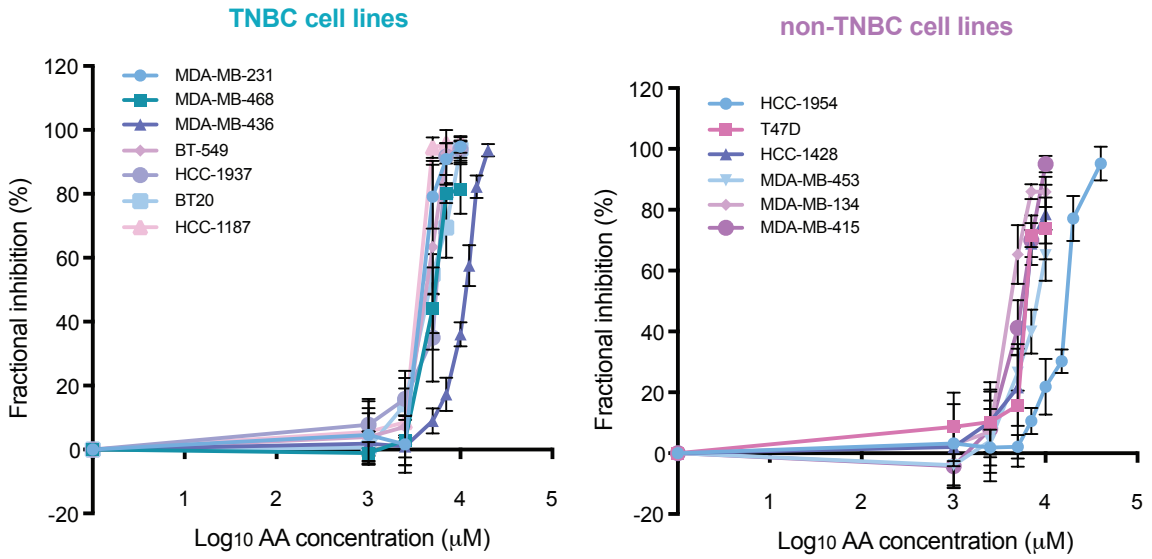
Top Networks

ID Associated Network Functions	Score
1. Cancer, Cell Death and Survival, Cellular Development	41
2. Carbohydrate Metabolism, Small Molecule Biochemistry, Nervous System Development and Function	37
3. Carbohydrate Metabolism, Small Molecule Biochemistry, Hereditary Disorder	34
4. Cell-to-Cell Signaling and Interaction, Cancer, Organismal Injury and Abnormalities	25
5. Cell Death and Survival, Organ Morphology, Tissue Development	23

B

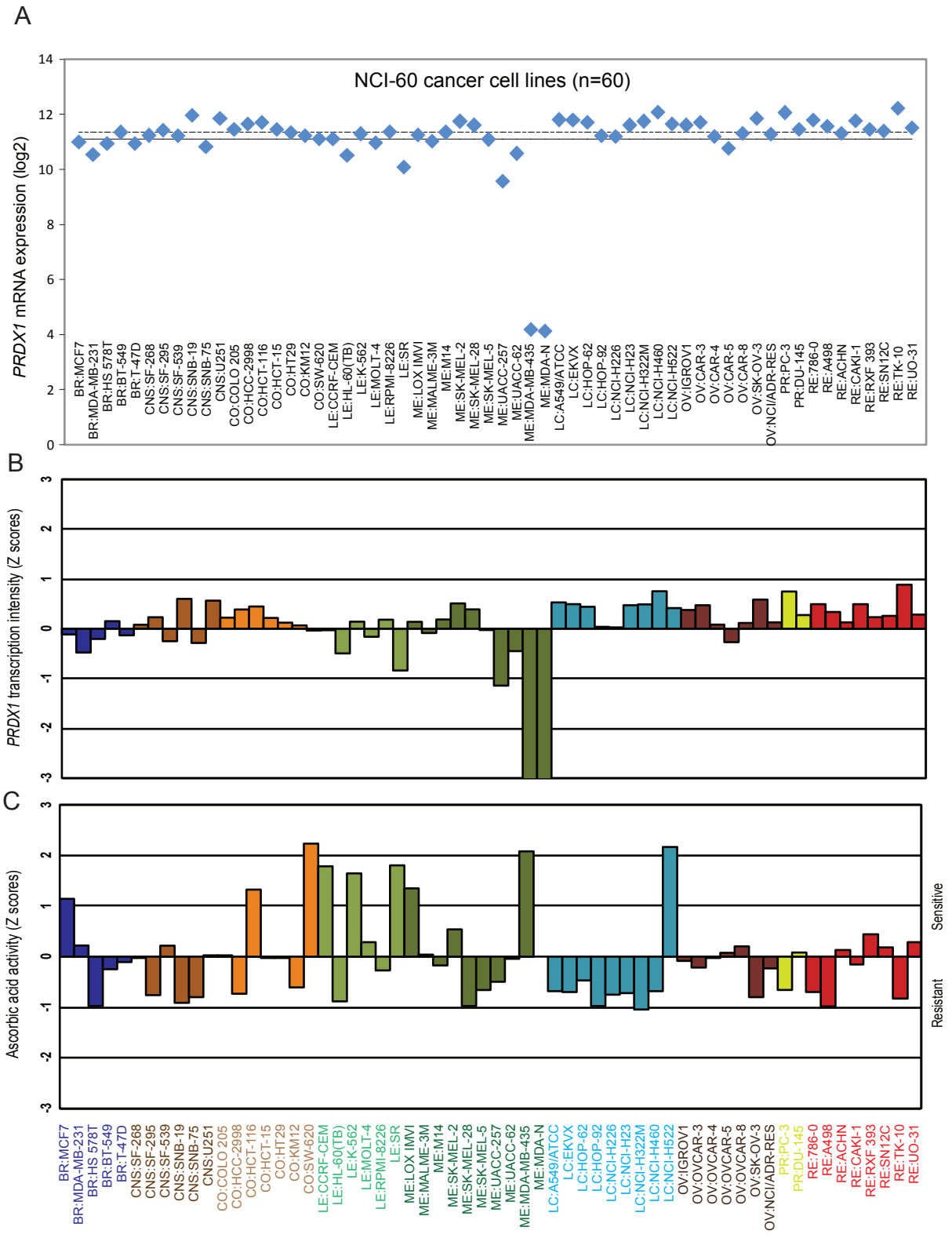


Supplementary Fig. 2. Classification of the genes/pathways that correlate with resistance to AA activity in NCI-60 cancer cells. Pattern comparison available at the NCI-60 CellMiner web tool (https://discover.nci.nih.gov/cellminer/) was used to assess the correlation between gene expression and AA (33832) activity. Significant negative Pearson's correlations are defined at $r < -0.334$ based on a minimum of 35 informative cell lines (for both forms of information) yielding P value < 0.05 in the absence of multiple comparisons. Expression of 246 genes correlates negatively and significantly with AA cytotoxicity (Pearson's correlations $r < -0.334$, P value < 0.05 in the absence of multiple comparisons). (A) Using the IPA, the 246 genes were classified. The top 5 significantly ($P < 0.05$) enriched canonical pathways, molecular and cellular functions and networks of these genes are represented. (B) These genes were mapped according to their GO biological process pathways in DAVID database. The top significantly ($P < 0.05$) associated biological processes were represented. *, $P < 0.05$; **, $P < 0.01$.



	MDA-MB-231	MDA-MB-468	MDA-MB-436	BT-549	HCC-1937	BT20	HCC-1187	HCC-1954	T47D	HCC-1428	MDA-MB-453	MDA-MB-134	MDA-MB-415
LogIC50 (μM)	3.624	3.693	4.081	3.655	3.724	3.766	3.518	4.216	3.75	3.757	3.925	3.615	3.792
IC50 (μM)	4208	4931	12037	4523	5302	5836	3298	17464	5619	5716	8421	4121	6196
95% Confidence Intervals (IC50) Bottom	-0.7069 to 3.932	-2.303 to 3.393	-0.3322 to 2.586	-3.573 to 8.461	4.873 to 9.894	-4.91 to 3.048	0.144 to 5.36	-0.251 to 6.527	2.564 to 9.785	0.2506 to 8.984	-5.315 to 0.5627	-2.247 to 5.446	-5.18 to 0.6338
95% Confidence Intervals (IC50) Top	90.35 to 96.52	76.61 to 89.55	103 to 124.7	87.51 to 106.9	89.57 to 99.09	97.5 to 199.1	93.46 to 98.73	95.45 to 114.5	67.08 to 82.19	71.95 to 87.56	74.65 to 646.9	82.94 to 93.74	104.9 to 153.3
R square	0.9789	0.96	0.9092	0.9213	0.9527	0.9685	0.9866	0.4177	0.8627	0.9251	0.9113	0.9403	0.9677

Supplementary Fig. 3. Sensitivity of TNBC and non-TNBC cell lines to AA. Seven TNBC cell lines (left panel) and 6 non-TNBC cells (right panel) were treated with increasing concentration of AA for 24 hours. Cell viability (%) relative to non-treated cells was measured with MTT assay. The graphs representing cell growth inhibition (100% – cell viability %) against log10 of AA concentration (μM). IC50 of each cell line, 95% confidence interval and R square were generated by GraphPad software. Data are means ± SD of at least 3 independent experiments.



Supplementary Fig. 4. *PRDX1* expression versus NCI-60 cancer cell response to AA. (**A**) *PRDX1* mRNA expression patterns (log2 values) using transcriptomic data of NCI-60 cancer cell lines. Mean and median values are shown as solid and dashed lines, respectively. (**B**-**C**) *PRDX1* mRNA expression patterns (average transcript intensity Z scores) (**B**) and AA activity (Z score). (**C**) in NCI-60 cancer cell lines. Cancer cells type is indicated in different colors, the cell line abbreviations are as follows: BR, breast; CNS, central nervous system; CO, colon; LE, leukemia; ME, melanoma; LC, lung cancer; OV, ovarian; PR, prostrate; RE, renal. Lung cancer cells (7/9 cancer cell lines) have high *PRDX1* expression and are mostly resistant to AA activity (8/9 cancer cell lines) (in blue). For other cancer types, the correlations between *PRDX1* expression and AA activity is not conclusive due to limited number of cell lines available for each cancer type.