

Supplementary Materials

Cisplatin resistance in head and neck squamous cell carcinoma is linked to DNA damage response and cell cycle arrest transcriptomics rather than poor drug uptake

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Supplementary Table 1. Changes in gene expression in HNO41 following cisplatin treatment

Gene name	Fold-change	log2 fold-change	P value
<i>GADD45G</i>	25.48	4.67129337248158	0.000387
<i>CDKN1A</i>	13.75	3.78135971352466	0.000000
<i>GADD45A</i>	12.83	3.68144926531496	0.000983
<i>PPP1R15A</i>	8.58	3.10097764772482	0.000337
<i>DDIT3</i>	2.88	1.52606881166759	0.000301
<i>H2AFX</i>	1.85	0.887525270741588	0.001314
<i>XPA</i>	-2.24	-1.163498732	0.00838
<i>REV1</i>	-2.01	-1.007195501	0.00079
<i>SIRT1</i>	1.7	0.765534746362977	0.000499
<i>ABL1</i>	-1.78	-0.831877241	0.008211
<i>ATR</i>	-1.23	-0.298658316	0.003974
<i>CDC25C</i>	-1.27	-0.344828497	0.006044
<i>CRY1</i>	-1.58	-0.659924558	0.001003
<i>RBBP8</i>	-1.58	-0.659924558	0.000598
<i>ATRIP</i>	1.09	0.124328135002202	0.373304
<i>BAX</i>	1.12	0.16349873228288	0.278637
<i>BBC3</i>	2.59	1.37295209791183	0.015325
<i>CDC25A</i>	1.17	0.22650852980868	0.229442
<i>CDK7</i>	1.07	0.0976107966264223	0.31912
<i>CIB1</i>	1.07	0.0976107966264223	0.129169
<i>ERCC1</i>	1.48	0.565597175854225	0.018632
<i>HUS1</i>	1.18	0.238786859587117	0.092654
<i>MBD4</i>	1.04	0.0565835283663675	0.22948
<i>MDC1</i>	1.06	0.0840642647884746	0.614952
<i>OGG1</i>	1.02	0.0285691521967709	0.809733
<i>PNKP</i>	1.05	0.070389327891398	0.544916
<i>PRKDC</i>	1.06	0.0840642647884746	0.126511
<i>RAD18</i>	1.02	0.0285691521967709	0.811874
<i>RAD51B</i>	1.06	0.0840642647884746	0.581671
<i>RAD9A</i>	1.04	0.0565835283663675	0.729851
<i>TP53</i>	1.04	0.0565835283663675	0.647312
<i>APEX1</i>	-1.16	-0.214124805	0.137984
<i>ATM</i>	-1.08	-0.111031312	0.287541
<i>ATRX</i>	-1.07	-0.097610797	0.528759
<i>BARD1</i>	-1.38	-0.464668267	0.053668
<i>BLM</i>	-1.26	-0.333423734	0.087956
<i>BRCA1</i>	-1.15	-0.201633861	0.124097
<i>BRIP1</i>	-1.26	-0.333423734	0.044348
<i>CHEK1</i>	-1.03	-0.042644337	0.813531
<i>CHEK2</i>	-1.34	-0.422233001	0.011496
<i>CSNK2A2</i>	-1.17	-0.22650853	0.145901

<i>DDB1</i>	-1	0	0.955514
<i>DDB2</i>	-1.19	-0.250961574	0.046844
<i>ERCC2</i>	-1.3	-0.378511623	0.179527
<i>EXO1</i>	-1.31	-0.389566812	0.019621
<i>FANCA</i>	-1.04	-0.056583528	0.714128
<i>FANCD2</i>	-1.12	-0.163498732	0.210433
<i>FANCG</i>	-1.17	-0.22650853	0.068444
<i>FEN1</i>	-1.07	-0.097610797	0.159901
<i>LIG1</i>	-1.19	-0.250961574	0.035381
<i>MAPK12</i>	-1.22	-0.286881148	0.083128
<i>MCPH1</i>	-1.33	-0.411426246	0.153643
<i>MLH1</i>	-1.13	-0.176322773	0.129506
<i>MLH3</i>	-1.23	-0.298658316	0.085196
<i>MPG</i>	-1.1	-0.137503524	0.281626
<i>MRE11</i>	-1.21	-0.275007047	0.229615
<i>MSH2</i>	-1.43	-0.516015147	0.02187
<i>MSH3</i>	-1.17	-0.22650853	0.09692
<i>NBN</i>	-1.1	-0.137503524	0.406568
<i>NTHL1</i>	-1.07	-0.097610797	0.139715
<i>PARP1</i>	-1.17	-0.22650853	0.180744
<i>PCNA</i>	-1.14	-0.189033824	0.092047
<i>PMS1</i>	-1.38	-0.464668267	0.045066
<i>PMS2</i>	-1.04	-0.056583528	0.816489
<i>PPM1D</i>	-1.15	-0.201633861	0.183088
<i>RAD1</i>	-1.08	-0.111031312	0.420389
<i>RAD17</i>	-1.4	-0.485426827	0.028869
<i>RAD21</i>	-1.22	-0.286881148	0.114037
<i>RAD50</i>	-1.38	-0.464668267	0.010565
<i>RAD51</i>	-1.38	-0.464668267	0.126268
<i>RNF168</i>	-1.05	-0.070389328	0.68359
<i>RNF8</i>	-1.18	-0.23878686	0.259498
<i>RPA1</i>	-1.17	-0.22650853	0.164612
<i>SMC1A</i>	-1	0	0.996634
<i>SUMO1</i>	-1.23	-0.298658316	0.069092
<i>TOPBP1</i>	-1.26	-0.333423734	0.021749
<i>TP53BP1</i>	-1.1	-0.137503524	0.248714
<i>TP73</i>	-1.34	-0.422233001	0.085635
<i>UNG</i>	-1.11	-0.150559677	0.148541
<i>XPC</i>	-2	-1	0.173518
<i>XRCC1</i>	-1.17	-0.22650853	0.128779
<i>XRCC2</i>	-1.2	-0.263034406	0.151687
<i>XRCC3</i>	-1.18	-0.23878686	0.424499
<i>XRCC6</i>	-1.01	-0.014355293	0.9066

Supplementary Table 2. Changes in gene expression in HNO97 following cisplatin treatment

Gene name	Fold-change	log2 fold-change	P value
<i>GADD45G</i>	16.2	4.0179219079	0.000002
<i>GADD45A</i>	8.29	3.05137210172	0.000181
<i>DDIT3</i>	7.75	2.9541963103	0.000033
<i>PPP1R15A</i>	4.75	2.2479275134	0.000025
<i>CDKN1A</i>	3.08	1.6229303509	0.000001
<i>SIRT1</i>	1.35	0.43295940727	0.003585
<i>REV1</i>	-3.13	-1.646162657	0.000054
<i>TP73</i>	-2.61	-1.384049807	0.000162
<i>MCPH1</i>	-2.48	-1.310340121	0.000038
<i>RBBP8</i>	-2.18	-1.124328135	0.000008
<i>PMS2</i>	-2.15	-1.10433666	0.001146
<i>ABL1</i>	-1.95	-0.963474124	0.000139
<i>APEX1</i>	-1.51	-0.59454855	0.000595
<i>ATRIP</i>	-1.36	-0.443606651	0.003099
<i>ATRX</i>	-1.93	-0.948600847	0.001113
<i>BARD1</i>	-1.61	-0.687060688	0.001161
<i>BAX</i>	-1.28	-0.35614381	0.000526
<i>BLM</i>	-1.88	-0.910732662	0.00113
<i>BRCA1</i>	-1.46	-0.545968369	0.002476
<i>BRIP1</i>	-1.51	-0.59454855	0.004445
<i>CDC25A</i>	-1.51	-0.59454855	0.001208
<i>CDC25C</i>	-1.96	-0.970853654	0.00022
<i>CDK7</i>	-1.28	-0.35614381	0.003006
<i>CHEK1</i>	-1.43	-0.516015147	0.000022
<i>CHEK2</i>	-1.65	-0.722466024	0.005388
<i>CIB1</i>	-1.25	-0.321928095	0.001125
<i>DDB1</i>	-1.62	-0.695993813	0.000528
<i>DDB2</i>	-1.72	-0.782408565	0.00017
<i>ERCC2</i>	-1.74	-0.799087306	0.008196
<i>EXO1</i>	-1.26	-0.333423734	0.004111
<i>FANCA</i>	-1.39	-0.475084883	0.007366
<i>FANCD2</i>	-1.56	-0.641546029	0.000098
<i>MAPK12</i>	-1.64	-0.713695815	0.000587
<i>MDC1</i>	-1.43	-0.516015147	0.000926
<i>MLH1</i>	-1.5	-0.584962501	0.000986
<i>MLH3</i>	-1.72	-0.782408565	0.000536
<i>MPG</i>	-1.35	-0.432959407	0.000437
<i>MRE11</i>	-1.78	-0.831877241	0.002638
<i>MSH2</i>	-1.6	-0.678071905	0.000038
<i>MSH3</i>	-1.7	-0.765534746	0.001327
<i>NTHL1</i>	-1.59	-0.669026766	0.003506

<i>OGG1</i>	-1.43	-0.516015147	0.000945
<i>PARP1</i>	-1.6	-0.678071905	0.000406
<i>PCNA</i>	-1.5	-0.584962501	0.001084
<i>PMS1</i>	-1.45	-0.5360529	0.001634
<i>PPM1D</i>	-1.99	-0.992768431	0.006315
<i>RAD1</i>	-1.36	-0.443606651	0.001086
<i>RAD17</i>	-1.49	-0.575312331	0.001149
<i>RAD21</i>	-1.76	-0.815575429	0.000262
<i>RAD50</i>	-1.52	-0.604071324	0.00074
<i>RAD51</i>	-1.59	-0.669026766	0.000788
<i>RNF168</i>	-1.59	-0.669026766	0.000825
<i>RNF8</i>	-1.84	-0.879705766	0.000577
<i>RPA1</i>	-1.56	-0.641546029	0.000129
<i>SMC1A</i>	-1.59	-0.669026766	0.002027
<i>SUMO1</i>	-1.58	-0.659924558	0.000205
<i>TOPBP1</i>	-1.85	-0.887525271	0.000198
<i>TP53</i>	-1.56	-0.641546029	0.001543
<i>TP53BP1</i>	-1.51	-0.59454855	0.000759
<i>XPC</i>	-1.91	-0.933572638	0.00935
<i>XRCC1</i>	-1.36	-0.443606651	0.000595
<i>XRCC2</i>	-1.97	-0.97819563	0.000153
<i>XRCC3</i>	-1.74	-0.799087306	0.004348
<i>XRCC6</i>	-1.4	-0.485426827	0.002289
<i>BBC3</i>	1.04	0.056583528	0.727172
<i>MBD4</i>	1.01	0.0143552929	0.886589
<i>UNG</i>	1.01	0.0143552929	0.812183
<i>ATM</i>	-1.21	-0.275007047	0.145606
<i>ATR</i>	-1.25	-0.321928095	0.12573
<i>CRY1</i>	-1.03	-0.042644337	0.603647
<i>CSNK2A2</i>	-1.36	-0.443606651	0.010399
<i>ERCC1</i>	-1.19	-0.250961574	0.010539
<i>FANCG</i>	-1.19	-0.250961574	0.037818
<i>FEN1</i>	-1.06	-0.084064265	0.355576
<i>H2AFX</i>	-1.17	-0.22650853	0.052745
<i>HUS1</i>	-1.99	-0.992768431	0.010741
<i>LIG1</i>	-1.39	-0.475084883	0.016336
<i>NBN</i>	-1.33	-0.411426246	0.084762
<i>PNKP</i>	-1.2	-0.263034406	0.010569
<i>PRKDC</i>	-1.22	-0.286881148	0.024583
<i>RAD18</i>	-1.36	-0.443606651	0.012273
<i>RAD51B</i>	-1.56	-0.641546029	0.01366
<i>RAD9A</i>	-1.19	-0.250961574	0.011807
<i>XPA</i>	-1.23	-0.298658316	0.154966

Supplementary Table 3. Baseline differences in gene expression between HNO97 and HNO41

Gene name	Fold-difference	log2 fold-difference	P value
<i>CDKN1A</i>	6.85	2.776103988	0.00008
<i>TP53</i>	6.29	2.653060017	0.000001
<i>OGG1</i>	6.20	2.632268215	0.000031
<i>FANCD2</i>	5.71	2.513490746	0.00001
<i>RAD18</i>	4.79	2.260025656	0.000014
<i>MCPH1</i>	4.39	2.13422094	0.000078
<i>NBN</i>	4.16	2.056583528	0.000042
<i>TOPBP1</i>	4.05	2.017921908	0.000000
<i>RAD50</i>	3.99	1.996388746	0.00002
<i>H2AFX</i>	3.74	1.90303827	0.000001
<i>CDK7</i>	3.41	1.769771739	0.000003
<i>REV1</i>	3.34	1.739848103	0.00002
<i>MBD4</i>	3.3	1.722466024	0.000032
<i>MSH3</i>	3.25	1.700439718	0.000028
<i>XRCC2</i>	3.23	1.691534165	0.000001
<i>FANCG</i>	3.15	1.655351829	0.000007
<i>TP73</i>	3.15	1.655351829	0.000112
<i>MRE11</i>	3.06	1.613531653	0.000081
<i>CDC25C</i>	2.92	1.545968369	0.000000
<i>SIRT1</i>	2.89	1.531069493	0.000012
<i>ERCC2</i>	2.83	1.500802053	0.001291
<i>ATM</i>	2.81	1.49057013	0.000216
<i>CHEK1</i>	2.76	1.464668267	0.000048
<i>DDB2</i>	2.68	1.422233001	0.000115
<i>FANCA</i>	2.65	1.40599236	0.000052
<i>UNG</i>	2.61	1.384049807	0.000191
<i>RAD17</i>	2.6	1.378511623	0.000878
<i>APEX1</i>	2.54	1.344828497	0.000105
<i>HUS1</i>	2.51	1.327687364	0.00249
<i>PCNA</i>	2.48	1.310340121	0.000048
<i>DDB1</i>	2.46	1.298658316	0.000288
<i>BRIP1</i>	2.45	1.292781749	0.000071
<i>MLH1</i>	2.35	1.232660757	0.000142
<i>EXO1</i>	2.34	1.22650853	0.000007
<i>BLM</i>	2.32	1.214124805	0.000059
<i>MSH2</i>	2.32	1.214124805	0.000215
<i>ABL1</i>	2.27	1.182692298	0.000063
<i>SUMO1</i>	2.19	1.13093087	0.000014
<i>RNF8</i>	2.18	1.124328135	0.000001
<i>MPG</i>	2.17	1.117695043	0.000417
<i>TP53BP1</i>	2.17	1.117695043	0.000125

<i>RAD21</i>	2.1	1.070389328	0.000028
<i>BAX</i>	2.09	1.063502942	0.000059
<i>XRCC3</i>	2.09	1.063502942	0.000461
<i>RAD51</i>	2.07	1.049630768	0.001334
<i>PPP1R15A</i>	2.03	1.021479727	0.000292
<i>ATR</i>	1.97	0.97819563	0.000153
<i>PMS1</i>	1.95	0.963474124	0.000687
<i>FEN1</i>	1.93	0.948600847	0.001967
<i>CDC25A</i>	1.82	0.86393845	0.000133
<i>CIB1</i>	1.8	0.847996907	0.001078
<i>RAD1</i>	1.79	0.839959587	0.000776
<i>ATRIP</i>	1.74	0.799087306	0.000154
<i>PPM1D</i>	1.71	0.773996325	0.005501
<i>BRCA1</i>	1.7	0.765534746	0.00002
<i>RPA1</i>	1.67	0.739848103	0.000495
<i>BARD1</i>	1.65	0.722466024	0.001227
<i>CHEK2</i>	1.56	0.641546029	0.001232
<i>RAD9A</i>	1.53	0.613531653	0.001417
<i>CRY1</i>	1.47	0.555816155	0.002395
<i>RNF168</i>	1.47	0.555816155	0.003449
<i>ATRX</i>	1.45	0.5360529	0.001331
<i>BBC3</i>	1.44	0.526068812	0.00793
<i>MDC1</i>	1.37	0.454175893	0.001416
<i>CSNK2A2</i>	1.29	0.367371066	0.006751
<i>LIG1</i>	1.27	0.344828497	0.008745
<i>XRCC1</i>	1.26	0.333423734	0.008077
<i>PMS2</i>	1.24	0.310340121	0.004569
<i>MLH3</i>	1.19	0.250961574	0.00852
<i>MAPK12</i>	-1.21	-0.27500704	0.001713
<i>PRKDC</i>	-1.55	-0.63226821	0.001129
<i>DDIT3</i>	-1.82	-0.86393845	0.00644
<i>RBBP8</i>	-3.08	-1.62293035	0.000067
<i>XPC</i>	1.51	0.59454855	0.290671
<i>SMC1A</i>	1.26	0.333423734	0.017661
<i>XRCC6</i>	1.44	0.526068812	0.040489
<i>RAD51B</i>	1.31	0.389566812	0.020054
<i>XPA</i>	1.3	0.378511623	0.018171
<i>GADD45G</i>	-1.56	-0.64154602	0.022591
<i>PARP1</i>	-1.2	-0.26303440	0.052422
<i>GADD45A</i>	1.06	0.084064265	0.817586
<i>ERCC1</i>	1.02	0.028569152	0.683046
<i>PNKP</i>	-1.02	-0.02856915	0.315587
<i>NTHL1</i>	-1.06	-0.08406426	0.386039