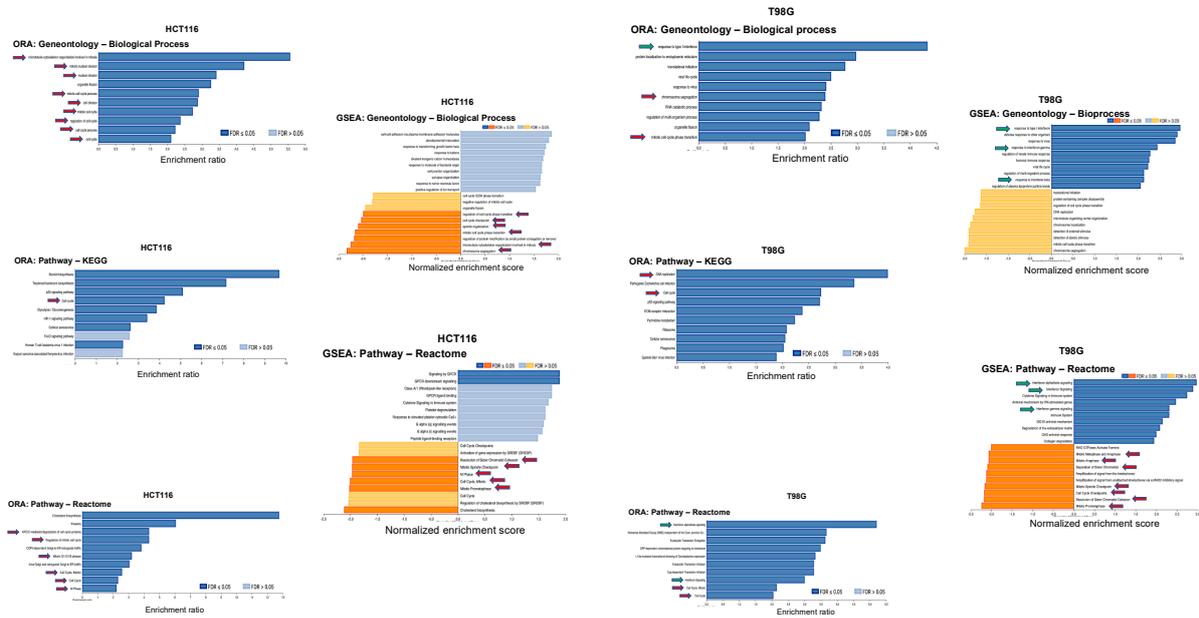


		HCT116	MDA-MB-231	T98	A375	A549	MCF7
<b>HCT116</b>							
	% NON-OVERLAP	45					
	% OVERLAP		26.8	11.6	2	39.1	5.60
	% OVERLAP NORMALIZED/1000 DEGS		15.1	15.5	8.7	10	13.8
		HCT116	MDA-MB-231	T98	A375	A549	MCF7
<b>MDA-MB-231</b>							
	% NON-OVERLAP		47.2				
	% OVERLAP	4.5		9.4	2.3	44.9	3.7
	% OVERLAP NORMALIZED/1000 DEGS	14.9		12.6	10	11.5	9.3
		HCT116	MDA-MB-231	T98	A375	A549	MCF7
<b>T98G</b>							
	% NON-OVERLAP			48.4			
	% OVERLAP	4.7	22.3		2.9	34	7.1
	% OVERLAP NORMALIZED/1000 DEGS	15.6	12.6		12.7	8.7	17.8
		HCT116	MDA-MB-231	T98	A375	A549	MCF7
<b>A375</b>							
	% NON-OVERLAP				54.1		
	% OVERLAP	2.6	17.9	9.6		31.4	12.7
	% OVERLAP NORMALIZED/1000 DEGS	8.6	10.1	12.9		8	31.8
		HCT116	MDA-MB-231	T98	A375	A549	MCF7
<b>A549</b>							
	% NON-OVERLAP					62.7	
	% OVERLAP	3	20.4	6.5	1.8		2
	% OVERLAP NORMALIZED/1000 DEGS	9.9	11.5	8.7	8		5
		HCT116	MDA-MB-231	T98	A375	A549	MCF7
<b>MCF7</b>							
	% NON-OVERLAP						51.3
	% OVERLAP	4.3	16.5	13.3	7.3	19.8	
	% OVERLAP NORMALIZED/1000 DEGS	14.2	9.3	17.8	31.7	5.04	

**Figure S1.** Dpep-responsive DEGs show both unique and overlapping patterns of expression in 6 cancer cell lines. Percentages of unique (highlighted in green) and overlapping (highlighted in yellow) Dpep-regulated DEGs among 6 different cancer lines are shown. Overlap comparisons are given based on absolute number and as normalized per 1000 DEGs to take into account the differing numbers of total DEGs observed in each line. Values highlighted in yellow designate the normalized percentages for A375 and MCF7 cells which are substantially higher than those for other cell line pairs.



**Figure S2.** ORA and GSEA geneontology and pathway analyses of total DEGs for HCT116 and T98G cells shows significant enrichment of DEGs related to various cell cycle events. Red arrows indicate categories relevant to various phases of the cell cycle. Green arrows indicate categories relevant to response to interferons.

# DEGs ASSOCIATED WITH DNA REPAIR

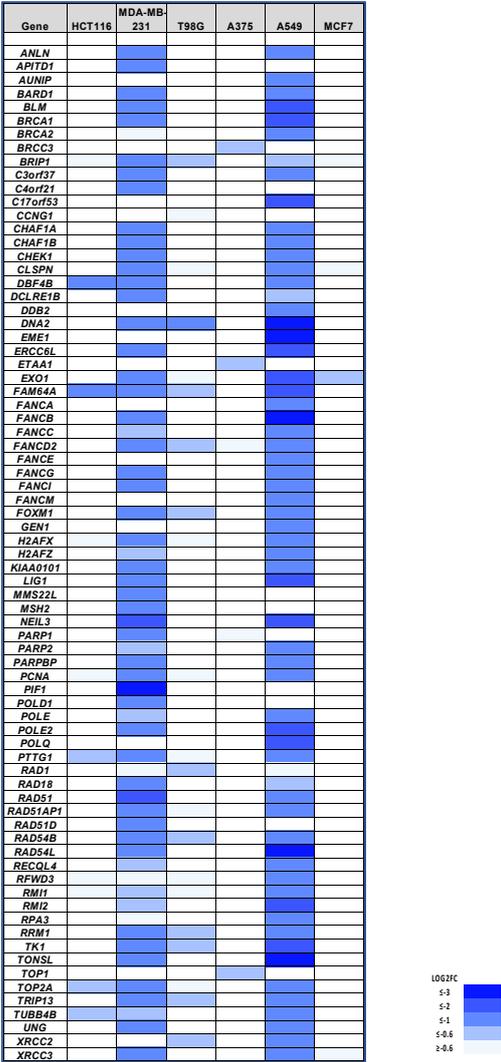
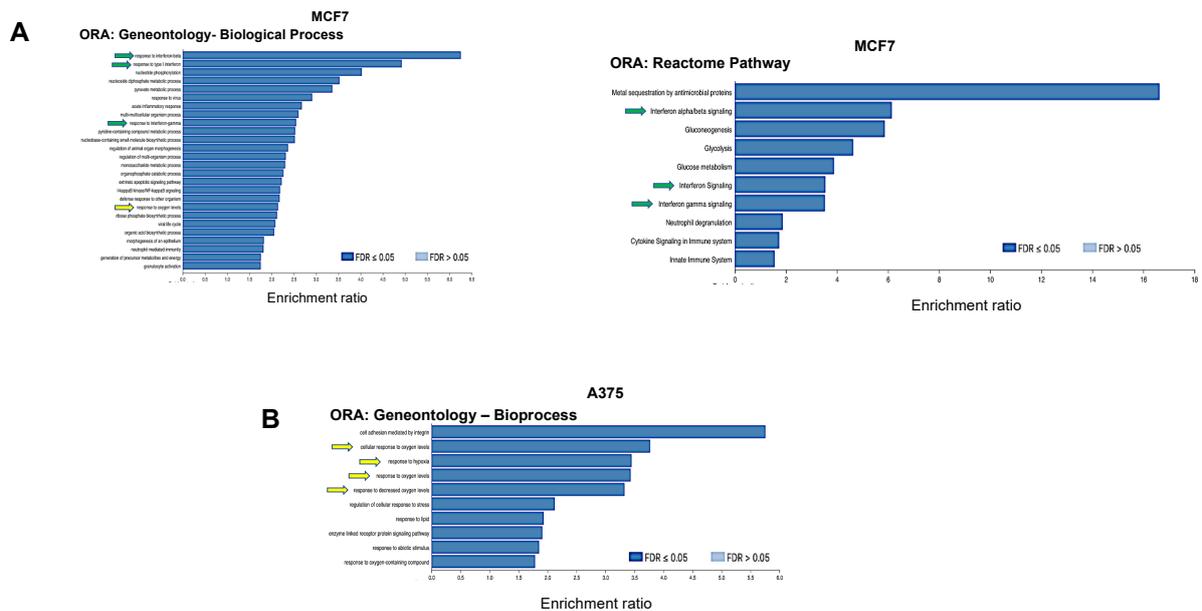


Figure S3. Dpep downregulates genes associated with DNA repair.



**Figure S4.** Dep regulates genes associated with interferon responses and hypoxia in a subset of cell lines. **A.** ORA geneontology and reactome analysis of MCF7 cell total DEGs reveals enrichment of genes associated with responses to interferons (green arrows) and hypoxia (yellow arrows). **B.** ORA geneontology analysis of A375 total DEGS reveals enrichment of genes associated with hypoxia (yellow arrows).

TUMOR SUPPRESSORS

ONCOGENES

A

Gene	HCT116	MDA-MB-231	T98G	A375	A549	MCF7
BATF2						
BDH2						
BTG1						
CDH13						
CDKN2A						
CDKN2B						
CLCA2						
CYP3A5						
CXXC4						
DDX58						
DEFB1						
DUSP6						
EBF3						
FBXW2						
FGF14						
FHIT						
GNG7						
IFI44L						
IFIT2						
IGFBP3						
IGFBP4						
IRF6						
LFNG						
LRIG3						
MAP3K5						
MPPE2						
NDRG1						
PRUNE2						
PCDH20						
PTPRU						
PTPRG						
RAB37						
RARRES1						
RBM4						
SELENBP1						
SEMA3B						
SPINK5						
TXNIP						
UNC5A						
XAF1						



B

Gene	HCT116	MDA-MB-231	T98G	A375	A549	MCF7
ATM						
BRCA1						
BRCA2						
CCNE1						
CCNE2						
CCNE3						
CCNE4						
CCNE5						
CCNE6						
CCNE7						
CCNE8						
CCNE9						
CCNE10						
CCNE11						
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CCNE98						
CCNE99						
CCNE100						



Figure S5. Dpep upregulates tumor suppressors and downregulates oncogenes with both context dependent and shared responses in multiple lines. A. Upregulated tumor suppressors. B. Down regulated oncogenes.

### HCT116

MEAN RANK				TOP RANK			
Rank	TF	Score	#Lines	Rank	TF	Score	#Lines
1	GMP	7.5	5	1	ETV7	6.14E-04	4
2	BATF2	15.33	4	2	BATF2	6.22E-04	3
3	RFX5	15.75	5	3	RFX5	7.12E-04	3
4	STAT1	24.87	3	4	STAT1	8.02E-04	4
5	RFX1	24.93	5	5	ABHL1	8.01245	2
6	STAT4	34.8	4	6	IKZF4	8.01423	2
7	SP119	41	2	7	TRAF3	8.01543	3
8	STAT3	45	5	8	ASCL2	8.01987	2
9	BHLHE40	48	6	9	ZNF384	8.02127	2
10	IRF8	57.93	2	10	IRF8	8.02287	2
11	PLSCR1	53.5	6	11	ZBED1	8.02429	3
12	NR1H3	55.5	5	12	THAP3	8.03071	2
13	SOX1	57.33	2	13	GMP	8.03111	5
14	NLF1	59.75	3	14	MNT	8.03387	2
15	SOX3	73.33	2	15	ZNF793	8.03561	2
16	NLF2	74	2	16	STAT2	8.03989	4
17	IRF8	75.5	5	17	ZNF229	8.03724	2
18	IRF3	78	2	18	RFX3	8.04274	2
19	IRF3	77.87	3	19	ZNF229	8.044	2
20	HMOX1	81.55	2	20	ETV6	8.04536	2
21	IRF8	81.87	3	21	AEBP1	8.04874	2
22	FOXP2	89.4	3	22	HMGN1	8.04973	2
23	ZNF35	106.3	2	23	FOXP1	8.04986	2
24	FOXP2	106.5	2	24	ZNF2	8.0506	2
25	SOX4	104	2	25	SOX2	8.05493	3
26	IRF8	109	2	26	SOX2	8.05523	2
27	ATF6B	107	2	27	RFX1	8.05724	4
28	IRF8	107.3	2	28	IRF8	8.05723	2
29	RFX1	107.4	4	29	PRDM2	8.05845	2
30	ZNF46	109.9	3	30	ZNF46	8.05973	2
31	IRF2B	116.7	2	31	PRKX2	8.07731	3
32	ZNF35	116.7	2	32	ZNF42	8.07847	2
33	ZNF35	116.5	3	33	SOX3	8.07933	2
34	SOX3	116.8	3	34	CBR1	8.07995	3
35	IRF8	117	2	35	SNAI1	8.08009	3
36	ZBED1	120.3	3	36	JUN	8.08473	4
37	SOX1	120.9	2	37	IRF8	8.08473	2
38	ZNF20	122	2	38	NCU1	8.08872	2
39	ZNF20	122.5	2	39	ZNF20	8.08872	2
40	STAT4	124.5	5	40	STAT4	8.09334	2
41	RFX1	127.5	2	41	ASCL2	8.09323	2
42	ZNF35	128.3	2	42	ZNF35	8.09398	5
43	STAT4	132.3	3	43	CEBPB	8.09372	5
44	HMOX1	134.3	2	44	HMOX1	8.09372	5
45	HMOX1	135.3	2	45	ZBTB14	8.10109	2
46	RFX1	139	2	46	RFX1	8.10109	3
47	ELK4	142.5	5	47	NR1H3	8.11109	4
48	STAT2	145.5	2	48	KLF11	8.11109	2
49	STAT2	145.5	2	49	KLF11	8.11109	2
50	BATF1	149	3	50	RFX5	8.12111	2
51	ATF5	155	2	51	ATF5	8.12111	2
52	CEBPB	155	2	52	CEBPB	8.12111	2
53	CEBPB	155	2	53	CEBPB	8.12111	2

### MDA-MB-231

MEAN RANK				TOP RANK			
Rank	TF	Score	#Lines	Rank	TF	Score	#Lines
1	GMP	7.5	5	1	ATF5	6.14E-04	4
2	CEBPB	15.33	4	2	RFX1	6.22E-04	2
3	CEBPB	15.75	5	3	RFX1	7.12E-04	2
4	ATF5	24.87	3	4	CEBPB	8.01229	3
5	RFX1	24.93	5	5	GMP	8.01423	5
6	RFX1	24.93	5	6	SOX2	8.01423	5
7	SOX2	34.8	4	7	SOX2	8.01543	3
8	RFX1	41	2	8	SOX2	8.01987	2
9	IRF8	45	5	9	GMP	8.02127	5
10	IRF8	48	6	10	JUN	8.02287	5
11	IRF8	57.93	2	11	JUN	8.02429	3
12	IRF8	53.5	6	12	ANZF2	8.02549	3
13	ZNF74	59.75	3	13	IRF8	8.02549	3
14	ZNF74	59.75	3	14	IRF8	8.02549	3
15	FOXP2	73.33	2	15	RFX1	8.02549	2
16	HMOX1	78	2	16	JUN	8.02549	3
17	ZNF35	81.55	2	17	IRF8	8.02549	3
18	ZNF35	81.55	2	18	IRF8	8.02549	3
19	ZNF35	81.55	2	19	ZNF474	8.02549	2
20	ZNF35	81.55	2	20	ZNF474	8.02549	2
21	ZNF35	81.55	2	21	FOXP2	8.02549	2
22	ZNF35	81.55	2	22	CEBPB	8.02549	2
23	ZNF35	81.55	2	23	CEBPB	8.02549	2
24	ZNF35	81.55	2	24	SOX2	8.02549	2
25	ZNF35	81.55	2	25	ZNF474	8.02549	2
26	ZNF35	81.55	2	26	PRKX2	8.02549	2
27	ZNF35	81.55	2	27	IRF8	8.02549	2
28	ZNF35	81.55	2	28	ZNF474	8.02549	2
29	ZNF35	81.55	2	29	ZNF474	8.02549	2
30	ZNF35	81.55	2	30	MNT	8.02549	2
31	ZNF35	81.55	2	31	ZNF474	8.02549	2
32	ZNF35	81.55	2	32	MNT	8.02549	2
33	ZNF35	81.55	2	33	MNT	8.02549	2
34	ZNF35	81.55	2	34	MNT	8.02549	2
35	ZNF35	81.55	2	35	MNT	8.02549	2
36	ZNF35	81.55	2	36	MNT	8.02549	2
37	ZNF35	81.55	2	37	MNT	8.02549	2
38	ZNF35	81.55	2	38	MNT	8.02549	2
39	ZNF35	81.55	2	39	MNT	8.02549	2
40	ZNF35	81.55	2	40	MNT	8.02549	2
41	ZNF35	81.55	2	41	MNT	8.02549	2
42	ZNF35	81.55	2	42	MNT	8.02549	2
43	ZNF35	81.55	2	43	MNT	8.02549	2
44	ZNF35	81.55	2	44	MNT	8.02549	2
45	ZNF35	81.55	2	45	MNT	8.02549	2
46	ZNF35	81.55	2	46	MNT	8.02549	2
47	ZNF35	81.55	2	47	MNT	8.02549	2
48	ZNF35	81.55	2	48	MNT	8.02549	2
49	ZNF35	81.55	2	49	MNT	8.02549	2
50	ZNF35	81.55	2	50	MNT	8.02549	2
51	ZNF35	81.55	2	51	MNT	8.02549	2
52	ZNF35	81.55	2	52	MNT	8.02549	2
53	ZNF35	81.55	2	53	MNT	8.02549	2
54	ZNF35	81.55	2	54	MNT	8.02549	2
55	ZNF35	81.55	2	55	MNT	8.02549	2
56	ZNF35	81.55	2	56	MNT	8.02549	2
57	ZNF35	81.55	2	57	MNT	8.02549	2
58	ZNF35	81.55	2	58	MNT	8.02549	2
59	ZNF35	81.55	2	59	MNT	8.02549	2
60	ZNF35	81.55	2	60	MNT	8.02549	2

### T98G

MEAN RANK				TOP RANK			
Rank	TF	Score	#Lines	Rank	TF	Score	#Lines
1	PLSCR1	3.8	6	1	PLSCR1	6.14E-04	3
2	BATF2	15.33	4	2	RFX1	6.22E-04	2
3	RFX1	15.75	5	3	ETV7	6.01229	4
4	RFX1	15.75	5	4	STAT1	7.12E-04	3
5	RFX1	15.75	5	5	STAT4	8.01423	4
6	RFX1	15.75	5	6	STAT4	8.01423	4
7	STAT4	24.87	3	7	BATF2	6.01987	4
8	ZNF251	24.93	3	8	BATF2	6.02289	2
9	BATF2	24.93	3	9	RFX1	8.02111	3
10	ARID3A	25.5	4	10	THAP3	8.02289	2
11	CEBPB	27.5	3	11	IRF8	8.02429	3
12	STAT1	27.87	2	12	NFKB1	8.02474	3
13	IRF8	28.5	5	13	RFX1	8.02474	3
14	GMP	33.5	5	14	MSC	8.02523	3
15	IRF8	34.8	4	15	RFX1	8.02549	2
16	NLF1	38	5	16	MSC	8.02588	2
17	STAT1	40.5	6	17	SOX2	8.02689	6
18	ATF5	40.83	2	18	ATF5	8.02689	2
19	JUNB	42.25	3	19	ZNF217	8.02723	2
20	SP4	44.83	2	20	SP4	8.02646	2
21	TWIST2	48.5	3	21	NFKB2	8.02737	3
22	IRF8	48	2	22	ARID3A	8.02787	2
23	BATF2	48.5	3	23	HNF1B	8.02833	2
24	JUN	48.83	2	24	LMNB2	8.02849	2
25	RFX1	50.25	2	25	NFKB1	8.02914	2
26	ATF5	51.25	2	26	MNT	8.02989	2
27	ATF5	51.25	2	27	ATF5	8.02989	2
28	RFX1	53.5	2	28	NFKB1	8.02989	2
29	STAT4	54.83	2	29	RFX1	8.02989	2
30	STAT4	54.83	2	30	RFX1	8.02989	2
31	STAT4	54.83	2	31	RFX1	8.02989	2
32	STAT4	54.83	2	32	RFX1	8.02989	2
33	STAT4	54.83	2	33	RFX1	8.02989	2
34	STAT4	54.83	2	34	RFX1	8.02989	2
35	STAT4	54.83	2	35	RFX1	8.02989	2
36	STAT4	54.83	2	36	RFX1	8.02989	2
37	STAT4	54.83	2	37	RFX1	8.02989	2
38	STAT4	54.83	2	38	RFX1	8.02989	2
39	STAT4	54.83	2	39	RFX1	8.02989	2
40	STAT4	54.83	2	40	RFX1	8.02989	2
41	STAT4	54.83	2	41	RFX1	8.02989	2
42	STAT4	54.83	2	42	RFX1	8.02989	2
43	STAT4	54.83	2	43	RFX1	8.02989	2
44	STAT4	54.83	2	44	RFX1	8.02989	2
45	STAT4	54.83	2	45	RFX1	8.02989	2
46	STAT4	54.83	2	46	RFX1	8.02989	2
47	STAT4	54.83	2	47	RFX1	8.02989	2
48	STAT4	54.83	2	48	RFX1	8.02989	2
49	STAT4	54.83	2	49	RFX1	8.02989	2
50	STAT4	54.83	2	50	RFX1	8.02989	2
51	STAT4	54.83	2	51	RFX1	8.02989	2
52	STAT4	54.83	2	52	RFX1	8.02989	2
53	STAT4	54.83	2	53	RFX1	8.02989	2
54	STAT4	54.83	2	54	RFX1	8.02989	2
55	STAT4	54.83	2	55	RFX1	8.02989	2
56	STAT4	54.83	2	56	RFX1	8.02989	2
57	STAT4	54.83	2	57	RFX1	8.02989	2
58	STAT4	54.83	2	58	RFX1	8.02989	2
59	STAT4	54.83	2	59	RFX1	8.02989	2
60	STAT4	54.83	2	60	RFX1	8.02989	2

### A375

MEAN RANK				TOP RANK			
Rank	TF	Score	#Lines	Rank	TF		