

Supplemental Material to:

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**Phospho- Δ Np63 α /microRNA feedback regulation in
squamous carcinoma cells upon cisplatin exposure**

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Supplemental Methods

Preparation of the nuclear extracts and DNA/protein binding. 5×10^9 cells (~140mg of total protein) were incubated with control medium or 10 μ g/ml cisplatin for 12h and the nuclear pellets were prepared and further incubated at a 250:1 ratio with poly (deoxyinosinic-deoxycytidylic) acid in 20mM HEPES-KOH (pH7.9), 1.5mM MgCl₂, 100mM NaCl, 0.1% (v/v) Nonidet P-40, and protease inhibitor mixture (Calbiochem) at room temperature for 10min, as described elsewhere.³¹ Resulting nuclear lysates were then incubated with MagnaBind streptavidin beads with the 25nmol bead-bound complementary double-stranded oligonucleotides (50bp) corresponding to the specific regions of the specific promoters for miR-181a-5p, miR-519a-3p, miR-374a-5p, miR-630 and miR-885-3p encompassing TP63 responsive element (Fig. 2, Fig. S1-S5). Double-stranded oligonucleotides were conjugated with MagnaBind™ streptavidin beads (Pierce).³¹ The concentration of conjugated DNA was 6fmol/ μ g of MagnaBind streptavidin beads.³¹ DNA/protein bead-bound complexes were washed with the binding buffer and bound proteins eluted using 100mM Tris-HCl (pH 7.3), 5mM EDTA, 0.05% SDS, and 8M urea at room temperature for 30min.³¹

iTRAQ labeling and fractionation by the strong cationic exchange (SCX) chromatography. For iTRAQ labeling, 200 μ g of eluted protein from large-scale DNA pull-downs were first subjected to gel-assisted digestion.²⁹ Trypsin digestion (20:1 (w/w) protein : trypsin) of gel samples were performed in 25mM TEABC at 37°C for 16h. Peptides were extracted from the gel using 50% acetonitril containing 5% (v/v) formic acid, vacuum dried, and reconstituted in 30 μ l of 25mM TEABC. To label peptides with the iTRAQ reagents (Applied Biosystems), one unit of labeling reagent (defined as the amount of reagent required to label 100 μ g of protein) was reconstituted in 70 μ l of ethanol. Products isolated from SCC-11 cells exposed to 10 μ g/ml cisplatin were labeled with

iTRAQ (115, 116 and 117), whereas products isolated from SCC-11M cells exposed to cisplatin were labeled with iTRAQ (113 and 114), respectively.²⁹ After incubation of specific mixes at room temperature for 1h, labeled peptides were pooled, resuspended in buffer A, and the specific mixes were fractionated by SCX chromatography on an Agilent HPLC system using a PolySulfoethyl A column.²⁹

Liquid chromatography (LC)/double mass spectrometry (MS/MS) analysis. Each SCX fraction were re-dissolved in 0.2% trifluoroacetic acid, desalted and separated on a C18 column with an 8 μ m emitter tip using 5-40% B (90% acetonitrile in 0.1% formic acid) gradient over 60min at 300nl/min. Eluting peptides were sprayed directly into an LTQ Orbitrap Velos mass-spectrometer (ThermoScientific) through an 1 μ m emitter tip at 1.6kV. Survey scans (full ms) were acquired from 350-1800 m/z with up to 10 peptide masses (precursor ions) individually isolated with a 1.2Da window and fragmented (MS/MS) using a collision energy of 45s and 30s dynamic exclusion.²⁹ Precursor and the fragment ions were analyzed at 30,000 and 7,500 respectively.

Data analysis. The MS/MS spectra were extracted and searched against the RefSeq 40 database and against the Swiss-Prot sequence database v54.2 using the MASCOT v2.2.1 program (Matrix Science) through Proteome Discoverer software (v1.1, Thermo Scientific). The peptides with a confidence threshold 5% False Discovery Rate (FDR) were identified based on a concatenated decoy database search). To calculate average protein ratios, the ratios of quantified unique iTRAQ peptides were weighted according to their peak intensities.²⁹ A protein's ratio is the median ratio of all unique peptides identifying the protein at a 5% FDR. The combination of two approaches was used to normalize the iTRAQ ratios: normalization by total protein (i.e. the average of all the ratios). Only proteins identified with ratios >1.25 or <0.75 were considered as potential targets.

Supplemental Legends

Figures 1-5. Schematic representation of the selected microRNA gene promoter sequences. Putative recognition sequences for tumor protein (TP) 53, TP63, sterol responsive element binding factor (SREBF), and nuclear factor (NF) -Y and other transcription factors are shown as bolded and shadowed boxes, while primers used for ChiP-PCR are underlined. Recognition sequences (responsive elements) defined using the web-based database: TFSEARCH: Searching Transcription Factor Binding Sites (version 1.3) (mbs.cbrc.jp/research/db/TFSEARCH.html). The following promoters depicted: S1 –miR-181a-5p; S2 – miR-519a-3p; S3- miR-374a-5p; S4 – miR-630; S5 – miR-885-3p.

Tables S1-S5. iTRAQ analysis of proteins bound to TP63 responsive element cognition sequence located in microRNA promoters induced by exposure of sensitive SCC-11 and resistant SCC-11M cells to cisplatin. Quantitative iTRAQ analysis was performed in triplicate. Protein complexes from the cells exposed to control medium were labeled with iTRAQ-113, or -114, while protein complexes from the cells exposed to cisplatin were labeled with iTRAQ-115, -116, or -117. Only proteins identified with iTRAQ ratios >1.3 or <0.7 were considered as potential differential interactors. S1 –miR-181a-5p; S2 – miR-519a-3p; S3- miR-374a-5p; S4 – miR-630; S5 – miR-885-3p.

-400 **CTAAGGTAAT** TCTGTTT**AAT TT**CTGTATAA G**CTATATAACA TAATGCTTGC**
SRY/OCT1 **CdxA** **XFD-1/TP63**
 -350 **TTACTATACG TGTAACAATA TT**TAA**AATTAT AAGATATTG**T TTGGATTTTA
TP63 **SOX5/CdxA** **CdxA/GATA3**
 -300 TACCACAAAG TACTTTG**AAT AACAA**ATTGT CCCTGTCTTT AACAGTGAGA
CdxA/SRY
 -250 **TAATTCAT**C TCTGGAACTA GC**CCAAT**ATC GGCC**ATGTTT TTGCTTGATG**
GATA1 **NF-Y** **FOXM1/TP63/OCT1**
 -200 **AAACAGG**TCC TTTTCTCTCA TACAATGTGA TGTGGA**GGTT TGCCAAACTC**
TP63/OCT1 **C/EBPβ**

Figure S2. Mir-519a-3p promoter sequence

-2000 **GTTTTGTTTG GTTGGTTATT TTT**GAGACAA **GGTCTGGCTC TGTCATCCAG**
SRY/FOXM1 C/EBP/CdxA **ZBTB6** **TP63**
 -1950 **G**CTGGAGTGT AGTGGTGTGA TCTCAGCTCA CTGCAACCTC CACCCCCGAC
 -1900 CTAAGCCTAC TGAATTA **GTG TCTACAGGCA CGCACTACCA CACCTGG**CTC
SREBF **TP63**
 -1850 ACTTTTGTAT TTTTTGTA**CA** **CATGGGGTTT CACATG** ATTG CCGGGGCTGG
E-box **TP53**
 -1800 TCTCAAAC**T**C **CTGTGCTCAG GTGATCCTCC** CATCACGGCC TCCT**AAAGTG**
TP63 **USF** **SREBF** **Nkx2**
 -1750 **CTGGAATTAG AGGTG**TGAGC CGCCACGC**CC CACCTGT**ACT TGTGTATCTC
POU3F1 **USF**
 -1700 TGTT**CAAATG** TTACTGAGGA GCTTTTACAG **CGTAACCTGT** GGTCTATCCT
E-box
 -1650 GGAA**AATGTT TGTGTGTGAG ACAATGTACA** TTCTTCAACA TCTTAGATTG
FOXD3 **C/EBP**
 -1600 CAGTTTGGAT GCTCCCGT**CA GGACTGTGTG TCCCTG**TGCT GGGACT**CAAG**
TP63 **E-box**
 -1550 **TG**AACACTGG GCTCTCCATC CATTGCTGTT GTCTAGAAAT CCAGC**CCAAT**
NF-Y
 -1500 TCTCTTGGGT **AAATAT**GAGG TATGTGTAGT AGGCATTGCT TTTTCTTTCT
CdxA
 -1450 GGAGACAAAG CT**CAGGAGGA TTGCCCTTG** AT**AAACAAA**G CTAACCTGCT
TP63 **SRY**
 -1400 GATTCTTTGA AGCAAGGAAC TGGAGATGGT CCTTTTAGGG GTTTATATTC
 -1350 TGGATTCCAG AAAACATGCA AA**CAGGACCA ATAAATGCGT G**CTTATTTTT
PBX1/TP63
 -1300 GTGTCTGTTT TAACCTGGTC AAGGAAAATT CCAACAAAAA ATCCACGATG
 -1250 CTGGAG**CATG AAGATCTCAG G**CTGTGTCCC TCTAGAGGGA AGCGCTTTCT
TP53
 -1200 GTTGTCTG**AA AGAAAAGAAA AT**GGTTCCTT TTAGAGTGTT ACGCTTTGAG
SRY/ RUNX1
 -1150 AAAAGCATCG CTGATCTTGG TAACACATTT GCAGAGAATG **CTTATAATCA**
OCT1
 -1100 **GACG**TGGATG ATGTTGAAGT TTTGC**GTTTG TTTTGTTTTG TTTTT**TTTCC
OCT1 **FOXD3** **FOXD3**
 -1050 TAGACAGGGT GTCTGCTGCC **CAACTG**AGAG TGCGGTGGCA CTTCCAACCT
E-box
 -1000 AGACCTCTTG GGT**TTAAGTG** GCCCTCTATT TT**GGGATAGA GT**CTTGCTCT
Nkx2 **IKZF1**
 -950 GTGGCC**CTGG CTGGAGTGCA GTGTCAGG**AA CTCTGCTCAC TGCGACCTCT
TP63
 -900 **GCCTCCTAGG TTCAAGCGAT** TCTCTTGCTT CAGCCTCCTG **AGCAGCTGGG**
Ik-2/E-box
 -850 **ATTA**CGGGCA TGTGCCACCA TGCCTGGCTA ATTTTTGTAT TTTTTATTAT
 -800 TT**ATTAT**TT **ATTAT**TTTT GAGACAGAGT CTCGCTCTGT CACCCAGGCT

CdxA CdxA
 -750 **GAAGTG**CAGT GGTGCGATCT TGGCTCACCG CAACCTCTAC CTCCACCTC
Nkx2
 -700 AGCCTCC**TGA ACAGCTGTCT** C**CAGGCGTGC ACCACCACAC CTGG**CTAACT
MyoD/E-box TP63 E-box
 -650 TCTGTATTTG TTTTACAGT**C ATGGTTTCAC CATG**TTGCC GGGCTCATCT
TP53
 -600 TGAACTCCTG AGC**TCAAGTG ATCCTCCC**GC CTCAGCCTCC TAAAGTGCTG
Nkx2/E-box/SREBF
 -550 TGAGCCACCG TGTCCCAACA GTACTTGTGT GTTTCCGTTT AAATTGTATT
 -500 GAGGAGCTTT TACAGCATAG CCTGTGGTCT CTCCGGG**AGA ATGTTTTTG**T
FOXD3
 -450 TTACGACAAT GTATATTCTT CAACATCGTA GATTCCATTT TGGATGCCCT
 -400 **CATTGGGACT GT**GTGTC**CCT GTACTGGAAC TCAAG**TGAA**C ACTTG**GCTCA
IKZF1 TP63/Nkx2 E-box

Figure S3. Mir-374a-5p promoter sequence

-2250 TTATCGAAGA GACTTCTAGA ATTAGTTATT TGTCAAAAGA TTTGAACATT
 -2200 ATAA**AGAATT GGCATATTTA CTTT**TCAA**AA AATT**AATGTC AGTTTTTGTA
OCT1/FOXM1 CdxA
 -2150 CCCAGTCC**ATT TAG**GTA**CTTA TAAAAA**AT**TGT TTTGCTTT**T TTTTTTTTT**G**
CdxA TATA FOXM1
 -2100 **CTGACTCCAT TTGTA**AAATGA ATGAATGATA TCTCTGTGGG GTTTTTTTTGT
TFAP1 YY1
 -2050 **TTTTGTTTTT TTC**TGAGA**CA GGCTCTCCCC CTG**TCGCCTA GG**CTGGAGTA**
FOXD3 TP63 TP63
 -2000 **CAGTGGCGTG ATTATG**GCTC ACTGAAGCCT **CCAAT**TCCAG GGCTCCAGAG
TP63 SREBF NF-Y
 -1950 ATCCTCCTAC CTCAGCCT**CC TGAGTAGCGG GAGTACAGG TGTGTGCC**ACC
TP63 E-box/TCF3
 -1900 **ATGTCCAGCT AATTTTTTAA** TTTTTTTTGT **AGAGATGGAG**T TTTGCCATGT
GATA1
 -1850 TGCT**CAGGCT TGTCTTGAAC TCCTGG**GC**TC AAGTGATTTT C**CCACCCCGG
TP63 Nkx2 SREBF
 -1800 CT**TCCCAAAA** **TGCTGGGATT ACAGGGGTGA GCCACCATAC CTGG**CCG**ATA**
STAT IKZF1 TP63
 -1750 **TCTTTGTTTT** GTGATACAGT TCTCTGATTA TTAGTGAGGC TGGACTTTTA
FOXM1
 -1700 GAT**CTTAATT AC**TAGC**TCTT ATTTCCTT**TT GTGAATTATT CAATTTGTGC
Nkx2 FOXM1
 -1650 CTGAATGTT**A TTTG**TAAGTT G**CAAATG**TCG TTTGTTGCAG ATATGCTCCC
CdxA E-box
 -1600 **AGTAATATTT GTTG** CCATTG **AGTCTGAAGA A**ATGTTTGCA ATTCCAAATA
CdxA FOXM1 C/EBPβ
 -1550 TAACTGCTGT GTGGATACAT GTCTGGTTCT T**GGTAGCCAT TTTGAGAT**AA
YY1
 -1500 **CATTTG**TCTG ACCTCTATCT TATTTTTTGT TTTATTTTTTA GAGTGGAGGT
E-box
 -1450 CTTGCC**CATG CTGGTCTCGA ACTCCTGGGC**TCAAGCAATC TTTCTGCCTC
TP53
 -1400 CGCCTCCCAA AG**TGCTGGGA TTAC**AGGCAT AAGCCACCTT ACCCAGCCTT
IKZF1
 -1350 GTC**TGACCTT TAAACA**GAAA TCCATTTCTT TTTATCTAAA AGGAAAGCAC
NR2F2
 -1300 TTTTGAGTAC TGTACAACAG TGGTGCTTCC TGGCC**CTGGG CATGGGGAGA**
TP63/MZF1
 -1250 **AGACAGG**GCA ACATTTTG**TC CCTAATGAGA A**ACTAATTTA GACAAGAAAC
TP63 OCT1
 -1200 **AAAACA**GCGG TCCCTTCTCC CCCAT**CCAAT** CAGGGACTGG TCTTATTTTA
SRY NF-Y

v-Myb

-800 **TT**CTTAGATT TCATTGTAA**C TGGACTGTT CAGG**TTGCCCA GAGGGAAAGA
TP63

-750 **ACATTCC**TAA TTCTAATAAA ATAAACTTTT ATTTTGTAT TCCATTAGTT
HSF1

-700 **ACTTATGTTT ATT**TTTATAG TTAAAAAATG ACTAAAGGTG GCTAATAGCC
FOXM1

-650 ACCCGTATTA TGTGCCTTAT TCACTGTTCC **CACTTAATAT AAAATGTCAA**
-600 AAATTGGTTG TTTCTTTGCA GGGAACTGTG **AATGAGCCCA TTCCCCAA****C**
STAT

-550 ATTTAACTT**G GTTAATGAAG CT**TTTCAGAGC ATTTTCTGAA AGATTTCCAA
OCT1

-500 TTTCTGCATC TCAGA**TATTG AATTAAATT GTTTGT**GTTG TAACAGTGAT
POU3F1 FOXD3

-450 **ACAAAAATGT TCAATAGCTC** TTTGAATGCC ACTTT**TTTTA AA**GAAAATAC
TATA

-400 **TTTTAAA**GTC ATTCTTAGCT AACCTCAAAA CTCCTTTACA TTACTTTCAT
TATA

-350 TTTAGCTCAC **TCTTAAAGCT GATACTGTTA** TATAGGGATG AAGGGAGAGT
-300 TTTCTTAAAG **AAGGTCCCAA AGTTGAAGAT** CGTTTGTCTAT TGATACTCTG
-250 GC**CAAGTCCA GGTTTTAGGA CATG**TTAATT TACTCTTATT TGGATCTGTA
TP53

Figure S5. Mir-885-3p promoter sequence

-2350 AGACTGGGTT **CCAAT**CCCAA CTCTACTCCT TAGCCAGGGA CCCCCAACAA
NF-Y

-2300 GCTTCCCCC CTTTCTGATT ATAGCCCCAG CTCATGAG**GT TGTGTTGAAA**
C/EBPβ

-2250 **TC**TGGAACCT CCAGAAATGT CCA**TTTCGCC** CTCTCATCCT TCATCT**CAAA**
E2F E-box

-2200 **TG**TCTCCCCT TTCCCACCTC TCTGGGCTAC CCCCTTCCCTC TTCATCATCC
-2150 AACTCCTCCC TACCTTCAG**C CTGCAGCAGC CTGCCTCCCC CAGGGGGTGT**
TP63 c-Rel

-2100 **TCC**TTGATTA GTTTCTTCCC CAGTGTCTG AACTCCCTGC ATAACAGC**CA**
-2050 **TTTG**GAT**GCT CATTTTTATG** **CA**CAACCAGA CACCATGGGC CCTTTACATC
E-box OCT1

-2000 **AGCGGGGA**GG CCTTGC**TGGG CTTCCA**GTC TGATGATC**CT TGAGGAACAA**
MZF1 c-Rel TP63

-1950 **CACAGAGAGA CCAGG**CTGGG GG**CATTGTG GTGT**CGTTAT GGTGGTTGAG
TP63 E-box ATF2

-1900 AAAGCCCTAG TGTCATCTCA TGCACGTGTTT CAGCTTAGAA GAGGGCAGGA
-1850 AACACTCCGC TCTGGT**CAGT TG**GTCCAACC ATGCTTGCC TGTGACCCTG
E-box

-1800 GACAGGTCCC TTCACCTCTC TGAGCCTCTG TGTCTGTGTC AGTGCAATGG
-1750 GGAAGCTGGT GAGGCCTCCA CTGCCTGCC **CACATGGCTG TTGTGGGGAC**
E-box/TP53/c-Myb/MZF1

-1700 **CACAGGCATG CACACGTG**TG ACTGTCCTTT GC**AAACAAA**C CCTGCGGTG
TP53 USF/E-box SRY

-1650 TGAGGTGCTG TATGGTGTGG AAGGAATGTG G**CATCTG**GAG GCAGAATGCC
E-box

-1600 CAGGTTCCAG CCCTCCAACA GCTCCCACTG TGGCCTCTGC CCCTCAGAAC
-1550 CTCAGTTTCC C**CATCTGACA AGTG**AGGGCA GACCAGCCTT CAGAAAGACT
E-box/Nkx2

-1500 CAAA**TGACCT CA**ACACT**CAG GGCACCAAGG AAATCATCAA AACCATG**CAG
ATF2 TP53

-1450 **GTTTCCCC**TA CCTTCCTACC CTC**CAGGGAC GGACAGG**CAG ACACGAGCCC
TCF3 TP53/TP63

-1400 ATGTCTGGTG TATCT**TCAA CGGG**ACAGAG TAAA**AATATT CAGAAATTG**C
v-Myb Oct-1/C/EBPβ

-1350 AAACATCATAT GTCTGCAGGG C**CAGGTAGG AGAGCACATG** **TCCTTTGGCC**

Description	Accession	MW [kDa]	5: 114/114	4/113	5: 115/115	115/115	116/116	116/116	115/115	117/117	117/117	pI	Coverage	# PS	Pept	Score A3	coverage	PSM	ptides
Table S1. Proteins interacting with the miR-181a-5p promoter sequence in SCC cells (11/11M) upon cisplatin exposure																			
tumor protein p63 [Homo sapiens], TP63	169234657	67.9	0.989	21	8.854	10	7.648	14	1.00	8.408	11	6.64	38.03	19	7	1528.45	53.03	31	12
histone deacetylase 4 [Homo sapiens], HDAC4	153085395	117.6	0.958	19	2.634	15	2.625	12	0.80	2.503	9	4.93	47.31	28	5	1295.89	47.31	15	5
nuclear transcription factor Y subunit alpha [Homo sapiens], NFYA	56417679	21.5	0.971	8	1.970	8	1.729	8	0.86	1.669	8	4.94	21.58	16	3	368.26	17.37	7	2
C-terminal-binding protein 1 isoform 1 [Homo sapiens], CTBP1	4557497	48.5	1.205	2	1.781	2	1.678	2	1.15	1.514	2	5.41	8.82	4	2	147.51	8.82	2	2
zinc finger and BTB domain-containing protein 2 [Homo sapiens], ZBTB2	24308241	61.0	0.909	4	1.718	4	1.527	4	0.97	1.611	4	4.98	11.16	5	8	542.97	9.13	15	6
SIN3 homolog B, transcription regulator [Homo sapiens], SIN3B	84569981	40.8	1.089	3	1.492	3	1.439	3	1.12	1.418	3	4.81	6.56	5	1	84.39	6.56	2	1
basic helix-loop-helix family, member e41 [Homo sapiens], SHARP1 (BHLHE41)	19684064	53.6	1.093	1	1.473	1	1.411	1	1.15	1.401	1	10.36	10.14	1	1	19.34	5.79	1	1
CCAAT/enhancer binding protein, beta [Homo sapiens], C/EBPbeta	119596035	40.1	1.137	8	1.446	8	1.280	8	0.93	1.503	8	8.22	13.24	13	7	243.76	9.00	5	5
methyl-CpG-binding protein 2 isoform 1 [Homo sapiens], MECP2	4826830	53.4	1.085	4	1.419	4	1.673	4	0.97	1.511	4	4.98	11.16	4	4	542.97	9.13	15	6
CCCTC-binding transcriptional repressor, isoform 1 [Homo sapiens], CTCF	5729790	80.8	1.048	13	1.303	14	1.319	14	1.97	1.302	14	6.07	12.45	12	7	354.67	11.45	24	9
Y-box binding protein 1 [Homo sapiens], YBX1	116283293	20.6	1.099	2	1.251	2	1.224	2	0.81	1.235	2	5.96	1.73	3	1	38.38	1.73	1	1
sex-determining region Y protein [Homo sapiens], SRY	383087989	23.6	0.905	18	1.217	57	1.380	17	1.18	1.263	17	8.84	32.74	14	16	2217.01	29.89	48	14
histone acetyltransferase KAT5 isoform 1 [Homo sapiens], KAT5	36287069	59.6	1.078	9	0.591	10	0.648	10	1.00	0.408	9	6.64	38.03	9	4	1926.45	38.03	34	9
CREB-regulated transcription activator 2 [Homo sapiens], CRTC2	32171215	77.5	0.916	29	0.581	29	0.625	29	0.80	0.503	29	4.93	47.31	28	5	535.89	47.31	15	5
histone-arginine methyltransferase [Homo sapiens] CARM1	40288288	66.5	1.135	4	0.322	4	0.348	4	0.81	0.236	4	8.35	13.43	6	5	367.22	11.51	11	4

Description	Accession	MW [kDa]	5:114/11	4:113	5:115/1	5:113	116/1	6:113	15/11	117/1	7:113	pI	Coverage	PSM	Pept	Score A3	coverage	SM	A	rides
Table SII. Proteins interacting with the miR-519-3p promoter sequence in SCC cells (1/11M) upon cisplatin exposure																				
tumor protein p63 [Homo sapiens], TP63	169234657	67.9	1.046	11	6.854	10	7.248	9	1.00	6.528	11	5.64	18.03	10	4	428.45	13.03	7	3	
histone deacetylase 1 [Homo sapiens], HDAC1	13128860	57.9	1.040	9	2.634	5	2.625	7	0.80	2.503	9	7.93	17.31	8	3	205.89	11.31	11	5	
SIN3 homolog B, transcription regulator [Homo sapiens], SIN3B	84569981	40.8	1.160	5	2.449	5	2.145	5	0.89	2.116	5	5.29	23.94	8	2	194.50	23.94	3	2	
nuclear transcription factor Y subunit alpha [Homo sapiens], NFYA	56417679	21.4	1.019	9	1.851	9	1.801	9	1.08	1.801	9	5.33	28.05	10	4	486.50	28.05	9	4	
BTG3 associated nuclear protein SMAR1 isoform a [Homo sapiens], BANP	17986266	55.3	1.016	5	1.807	5	1.406	5	0.89	1.612	5	5.29	23.94	8	2	194.50	23.94	3	2	
forkhead box D3 [Homo sapiens], FOXD3	6912372	52.5	0.931	1	1.731	1	1.641	1	1.15	1.440	1	10.36	10.14	1	1	19.34	5.79	1	1	
C-terminal-binding protein 1 [Homo sapiens], CTBP1	4557497	48.1	0.538	1	1.476	1	1.208	1	1.13	1.515	1	11.41	11.72	2	1	78.53	11.72	1	1	
sex-determining region Y protein [Homo sapiens], SRY	383087989	23.6	0.943	1	1.397	1	1.208	1	0.90	1.309	1	5.76	1.86	2	1	62.89	1.86	1	1	
basic helix-loop-helix family, member e41 [Homo sapiens], SHARP1 (BHLHE41)	19684064	53.6	1.243	2	1.368	2	1.485	2	0.97	1.216	2	6.33	16.56	52	6	764.68	16.56	24	6	
CCCTC-binding transcriptional repressor, isoform 1 [Homo sapiens], CTCF	5729790	80.8	1.043	13	1.311	14	1.219	14	1.10	1.302	14	6.07	16.97	50	8	570.77	15.51	21	7	
CCAAT/enhancer binding protein, beta [Homo sapiens], C/EBPbeta	119596035	40.1	1.079	5	1.245	5	1.370	5	0.85	1.216	5	5.64	5.48	8	3	425.91	5.48	5	3	
zinc finger and BTB domain-containing protein 2 [Homo sapiens], ZBTB2	24308241	61.2	0.755	2	1.232	2	1.425	2	1.03	1.399	2	6.80	5.94	4	2	108.46	5.94	2	2	
CREB-regulated transcription activator 2 [Homo sapiens], CRTC2	32171215	77.5	0.916	29	0.681	29	0.625	29	0.80	0.713	29	4.93	47.31	38	5	535.89	47.31	15	5	
histone acetyltransferase KAT2B [Homo sapiens], KAT2B	40805843	91.1	0.961	1	0.377	1	0.550	1	0.98	0.413	1	6.33	3.49	3	2	67.48	3.49	2	2	

Description	Accession	MW [kDa]	pI	114/1	115/1	116/1	117/1	118/1	119/1	120/1	121/1	122/1	123/1	124/1	125/1	126/1	127/1	128/1	129/1	130/1	131/1	132/1	133/1	134/1	135/1	136/1	137/1	138/1	139/1	140/1	141/1	142/1	143/1	144/1	145/1	146/1	147/1	148/1	149/1	150/1
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Table SIII. Proteins interacting with the miR-374a-5p promoter sequence in SCC cells (11/11M) upon cisplatin exposure

tumor protein p63 [Homo sapiens], TP63	169234657	67.9	0.985	50	7.518	51	7.744	51	0.87	8.841	51	5.59	53.03	103	7	1528.96	53.03	46	6
forkhead box D3 [Homo sapiens], FOXD3	6912372	52.6	1.153	17	1.726	17	2.042	17	0.85	1.351	17	5.38	47.45	27	6	528.50	40.88	11	5
sex-determining region Y protein [Homo sapiens], SRY	383087989	23.6	0.800	12	1.587	12	1.386	12	1.14	1.728	12	8.24	7.16	21	4	384.84	7.16	9	4
transcription factor AP-4 (activating enhancer binding protein 4) [Homo sapiens], TFAP4	4507447	43.2	0.956	1	1.558	1	1.290	1	0.90	1.352	1	6.80	1.25	2	1	46.78	1.25	1	1
CCAAT/enhancer binding protein, beta [Homo sapiens], C/EBPbeta	119596035	40.6	1.053	27	1.556	28	1.546	28	1.01	1.750	28	8.02	27.58	70	9	1373.71	26.32	34	8
forkhead box M1 isoform 1 [Homo sapiens], FOXM1	42544167	93.1	0.976	10	1.526	10	1.559	10	0.98	1.695	10	4.88	26.27	10	4	161.57	13.56	5	2
nuclear transcription factor Y subunit alpha, isoform 1 [Homo sapiens], NFYA	4505389	39.5	0.971	8	1.497	8	1.273	8	0.86	1.546	8	4.94	21.58	16	3	368.26	17.37	7	2
YY1 transcription factor [Homo sapiens], YY1	4507955	51.1	1.023	38	1.385	38	1.262	38	0.96	1.480	38	11.62	29.41	69	7	948.85	29.41	33	7
histone deacetylase 2 [Homo sapiens], HDAC2	46623327	137.9	1.084	21	1.350	21	1.531	21	0.88	1.558	21	6.98	27.53	33	7	579.47	25.00	17	6
CCCTC-binding transcriptional repressor, isoform 1 [Homo sapiens], CTCF	5729790	83.8	1.197	1	1.309	1	1.451	1	0.90	1.296	1	7.20	2.59	2	1	31.94	2.59	1	1
general transcription factor IIB [Homo sapiens], GTF2B	4504193	38.8	1.229	2	0.744	2	0.638	2	0.89	0.594	2	9.76	10.88	2	2	57.71	6.22	1	1
CREB-regulated transcription coactivator 2 [Homo sapiens], CTCR2	32171215	77.6	1.088	4	0.460	4	0.427	4	1.15	0.383	4	6.05	7.41	7	2	266.39	7.41	4	2
Sp1 transcription factor [Homo sapiens], Sp1	38372901	90.8	1.317	1	0.403	1	0.557	1	0.84	0.459	1	6.18	3.95	2	2	109.86	2.40	1	1
Cbp/p300-interacting transactivator 2, isoform 1 [Homo sapiens], CITED2	19923343	31.6	1.004	16	0.372	16	0.310	16	1.16	0.421	16	8.53	11.13	21	11	417.44	8.40	12	8
transcription factor AP-2 alpha (activating enhancer binding protein 2 alpha) [Homo sapiens], TFAP2A	109389358	45.3	1.049	1	0.219	1	0.293	1	0.94	0.258	1	7.75	3.01	2	1	51.61	3.01	1	1

Description	Accession	MW [kDa]	AS: 114/113	S: 114/113	AS: 115/111	S: 115/111	AS: 116/113	S: 116/111	115/116	AS: 117/113	S: 117/113	pI	Coverad	EPMS	Peptide	Score A3	Coverage A3	PSM A3	Peptides A
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Table SIV. Proteins interacting with the miR-630 promoter sequence in SCC cells (11/11M) upon cisplatin exposure

tumor protein p63 [Homo sapiens], TP63	169234657	67.9	0.987	21	7.369	21	6.753	21	0.81	6.999	21	6.16	50.05	20	8	1529.55	49.01	19	7
nuclear transcription factor Y, beta [Homo sapiens], NFYB	5453780	25.6	1.035	10	2.724	10	2.350	10	0.84	0.272	10	8.29	15.35	16	4	407.44	182.40	12	4
CREB-regulated transcription coactivator 2 [Homo sapiens], CRTC2	32171215	77.5	0.753	6	2.171	6	2.078	6	0.90	2.463	6	8.66	3.02	12	2	221.79	1.51	5	1
DNA damage-inducible transcript 3 [Homo sapiens], DDIT3	304282231	20.3	0.974	2	2.107	2	1.971	2	1.00	2.142	2	4.92	1.25	20	3	285.28	1.00	9	2
heat shock transcription factor 1 [Homo sapiens], HSF1	15779147	59.5	0.974	2	1.865	2	1.471	2	1.00	1.544	2	4.92	1.25	2	3	285.28	1.00	9	2
transcription factor Sp1, isoform a [Homo sapiens], SP1	38372901	92.4	0.953	7	1.724	7	1.325	7	0.93	1.537	7	6.92	10.61	13	2	173.50	10.61	6	2
transcription factor AP-2alpha, isoform a [Homo sapiens], TFAP2A	4507441	48.5	1.053	27	1.596	28	1.246	28	1.01	1.250	28	8.02	27.58	30	9	1373.71	26.32	34	8
v-myb myeloblastosis virus oncogene homolog [Homo sapiens], c-MYB	71682821	69.8	0.916	1	1.538	1	1.411	1	0.83	1.352	1	7.01	49.03	1	1	3911.15	38.41	1	1
general transcription factor IIB [Homo sapiens], GTF2B	18088837	36.5	0.953	6	1.417	6	1.380	6	0.90	1.463	6	8.66	3.02	12	2	221.79	1.51	5	1
histone acetyltransferase, KAT2B [Homo sapiens], KAT2B	40805843	94.6	0.982	1	1.392	1	1.473	1	1.02	1.432	1	4.67	6.79	5	6	712.45	6.56	3	2
Cbp/p300-interacting transactivator 2 isoform 1 [Homo sapiens], CITED2	19923343	31.6	0.968	1	1.358	1	1.276	1	1.15	1.276	1	6.13	3.15	2	1	66.61	3.15	1	1
TATA-binding protein-like protein 1 [Homo sapiens], TBPL1	358439409	21.6	0.905	3	1.247	3	1.329	3	1.10	1.555	3	5.12	5.14	4	2	84.19	2.86	1	1
activating transcription factor 2 [Homo sapiens], ATF2	120660330	57.8	0.933	2	1.228	2	1.248	2	0.81	1.530	2	7.03	51.92	4	4	5402.07	51.92	4	4
C-terminal-binding protein 1 isoform 1 [Homo sapiens], CTBP1	4557497	48.3	0.913	1	0.525	1	0.428	1	0.90	0.562	1	9.28	35.37	4	2	148.28	35.37	3	2
histone deacetylase 1 [Homo sapiens], HDAC1	49456395	53.6	0.904	16	0.347	16	0.390	16	1.16	0.472	16	8.53	11.13	16	11	417.44	8.40	12	8
histone-lysine N-methyltransferase EZH2 isoform b [Homo sapiens], EZH2	23510384	78.3	0.913	11	0.327	11	0.353	11	1.02	0.343	11	6.32	10.25	10	8	549.55	9.21	9	7
SIN3 homolog B, transcription regulator [Homo sapiens], SIN3B	84569981	40.8	1.189	4	0.315	3	0.344	3	1.12	0.379	3	4.81	6.56	5	1	84.39	6.56	2	1
CCCTC-binding transcriptional repressor, isoform 1 [Homo sapiens], CTCF	5729790	80.8	0.948	3	0.280	14	0.319	14	1.97	0.302	14	6.07	12.45	12	7	354.67	11.45	24	9

Description8	Accession	MW [kDa]	AS: 114/113	5: 114/113	AS: 115/111	5: 115/111	AS: 116/113	5: 116/111	115/116	AS: 117/113	5: 117/113	pI	Coverage	PSMs	Peptide	Score A3	Coverage A3	PSM A3	Peptides A3
Table SV. Proteins interacting with the miR-885-3p promoter sequence in SCC cells (11/11M) upon cisplatin exposure																			
tumor protein p63 [Homo sapiens], TP63	169234657	67.9	1.009	11	6.371	11	7.278	11	1.19	7.146	11	6.36	1.79	12	11	121.89	1.81	11	10
histone acetyltransferase, EP300 [Homo sapiens], KAT3B	50345997	271.3	1.013	1	2.757	1	2.828	1	1.02	2.328	1	5.76	5.33	2	2	108.85	5.39	3	2
Cbp/p300-interacting transactivator 2 isoform 1 [Homo sapiens], CITED2	19923343	31.6	1.018	1	2.135	1	2.086	1	0.97	2.065	10	6.62	22.65	1	1	504.31	18.58	1	1
CREB-regulated transcription coactivator 2 [Homo sapiens], CRTC2	32171215	77.5	0.908	6	1.942	6	1.813	6	1.16	1.629	6	7.96	8.82	7	4	137.17	8.82	4	4
TATA-binding protein-like protein 1 [Homo sapiens], TBPL1	358439409	20.5	0.976	24	1.931	24	1.558	24	1.00	1.719	24	7.55	16.96	42	11	1010.36	14.80	18	8
c-Rel homolog [Homo sapiens], c-REL	219518044	65.4	1.149	5	1.833	5	1.609	5	0.87	1.420	5	5.40	15.43	35	7	655.12	15.43	17	7
transcription factor Sp3, isoform 1 [Homo sapiens], SP3	38373693	88.5	0.929	16	1.794	15	1.750	15	1.08	1.649	16	5.66	17.84	48	14	1042.57	14.71	20	10
transcription factor AP2alpha, isoform a [Homo sapiens], TFAP2A	4507441	49.5	1.071	6	1.766	6	1.676	6	1.07	1.685	6	8.18	4.86	6	2	50.73	2.16	1	1
general transcription factor 2B [Homo sapiens], GTF2B	4504193	36.6	0.991	4	1.573	4	1.629	4	0.91	1.675	4	8.60	3.06	7	3	186.38	2.46	3	2
activating transcription factor 2 [Homo sapiens], ATF2	120660330	56.5	0.988	40	1.351	40	1.376	40	0.92	1.331	40	9.38	15.32	72	16	1292.39	13.47	36	13
DNA-damage-inducible transcript 3 [Homo sapiens], DDIT3	304282231	20.6	0.915	6	1.311	6	1.343	6	0.86	1.372	6	5.19	17.05	8	5	200.39	17.05	5	5
nuclear transcription factor Y, beta [Homo sapiens], NFYB	5453780	22.7	0.908	5	1.299	5	1.337	5	0.95	1.510	5	6.34	27.78	9	1	1590.80	27.78	4	1
histone-lysine N-methyltransferase EZH2 isoform a [Homo sapiens], EZH2	21361095	83.3	0.913	11	0.567	11	0.653	11	1.02	0.430	11	6.32	10.25	10	8	549.55	9.21	9	7
histone deacetylase 4 [Homo sapiens], HDAC4	153085395	117.6	0.753	6	0.337	6	0.278	6	0.90	0.463	6	8.66	3.02	12	2	221.79	1.51	5	1
C-terminal-binding protein 1 isoform 1 [Homo sapiens], CTBP1	4557497	48.3	1.091	1	0.257	1	0.283	1	0.90	0.328	1	9.28	35.37	4	2	148.28	35.37	3	2
SIN3 homolog B, transcription regulator [Homo sapiens], SIN3B	84569981	40.8	0.989	6	0.239	4	0.214	4	0.92	0.279	4	4.81	8.16	5	2	45.39	8.16	4	2