Title: CIC-DUX4 oncoprotein drives sarcoma metastasis and tumorigenesis via distinct regulatory programs

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Supplementary material contains the supplemental methods, 8 figures, and 4 tables.

Supplemental Methods.

Orthotopic and subcutaneous soft tissue xenografts in immunodeficient mice. Six to eight-week old female SCID mice were purchased from Taconic (Germantown, NY).

To prepare cell suspensions for quadriceps injection, adherent tumor cells were briefly trypsinized, quenched with 10% FBS DMEM media and resuspended in PBS. Cells were pelleted again and mixed with Matrigel matrix (BD Bioscience 356237) on ice for a final concentration of $1.0x10^5$ cells/µl. The Matrigel-cell suspension was transferred into a 1ml syringe and remained on ice until the time of implantation.

For orthotopic injection, mice were placed in the right lateral decubitus position and anesthetized with 2.5% inhaled isoflurane. A 0.5 cm surgical incision was made along the posterior medial line of the left hindlimb, fascia and adipose tissue layers were dissected and retracted to expose the quadriceps femoris muscle. A 30-guage hypodermic needle was used to advance through the muscular capsule. For all cell lines, care was taken to inject 10µl (1.0x10⁶ cells) of cell suspension directly into the left quadriceps femoris. The needle was rapidly withdrawn and mice were observed for bleeding. Visorb 4/0 polyglycolic acid sutures were used for primary wound closure of the fascia and skin layer. Mice were observed post-procedure for 1-2 hours and body weights and wound healing were monitoring weekly. For subcutaneous xenotransplantation, 3.0x10⁶ NCC_CDS1_X3 cells were resuspended in 50% PBS/50% Matrigel matrix and injected into the flanks of immunodeficient mice.

In-vivo bioluminescence imaging. Mice were imaged at the UCSF Preclinical Therapeutics Core starting on post-injection day 7 with a Xenogen IVIS 100 bioluminescent imaging system. Prior to imaging, mice were anesthetized with isoflurane and intraperitoneal injection (IP) of 200µl of D-Luciferin at a dose of 150mg/kg body weight was administered. Weekly monitoring of bioluminescence of the engrafted hindlimb tumors was performed until week 5. Radiance was calculated automatically using Living Image Software following demarcation of the left hindlimb (ROI). The radiance unit of photons/sec/cm2/sr is the number of photons per second that leave a square centimeter of tissue and radiate into a solid angle of one steradian (sr).

Ex-vivo bioluminescence imaging. Mice were injected IP with 200 μl (150mg/kg) of D-Luciferin and subsequently sacrificed at 5 weeks, en-bloc resection of the heart and lungs was performed. The heart was removed and the lungs were independently imaged. Imaging was performed in a 12 well tissue culture plate with Xenogen IVIS 100 bioluminescent imaging.

Cell lines and culture reagents. Cell lines were cultured as recommended by the American Type Culture Collection (ATCC). NIH-3T3, 293T, A673, RD, and RH30 cells were obtained from ATCC. NCC_CDS1_X1 and NCC_CDS_X3 were obtained from Tadashi Kondo at the National Cancer Center, Tokyo, Japan. The presence of the CIC-DUX4 fusion was confirmed through RNAseq analysis using the "grep" command as previously described (Panagopoulos et al, Plos One 2014). All cell lines were maintained at 37 °C in a humidified atmosphere at 5%

CO₂ and grown DMEM 1640 media supplemented with 10% FBS, 100 IU/ml penicillin and 100ug/ml streptomycin. Dinaciclib, palbociclib, SNS-032 were purchased from SelleckChem.

Gene knockdown and over-expression assays. All shRNAs were obtained from Sigma Aldrich. Sequences for individual shRNAs are as follows:

shETV4a: catalog # TRCN0000055132.

shETV4b: catalog # TRCN0000295522.

shCCNE1a: catalog # TRCN0000222722

shCCNE1b: catalog # TRCN0000077776

shCCNE1b: catalog # TRCN0000077777

ON-TARGET plus ETV4, ETV1, ETV5, Scramble, CDK1, CDK2, CDK7, CDK9, CCNE1, and CCNE2 siRNA were obtained from GE Dharmacon and transfection performed with Dharmafect transfection reagent. The HA-tagged CIC-DUX4 plasmid was obtained from Takuro Nakamura (The Cancer Institute of Japanese Foundation for Cancer Research, Tokyo, Japan). Sequence verification was performed using sanger sequencing. The lentiviral GFP-Luciferase vector was a kind gift from Michael Jensen (Seattle Children's Research Institute, Seattle, WA). Fugene 6 transfection reagent was used for all virus production and infection was carried out with polybrene.

Chromatin immunoprecipitation and PCR. CIC null cells (H1975 M1) were transfected with either GFP control, wild-type CIC, or CIC-DUX4 for 48 hours. SimpleCHIP Enzymatic Chromatin IP Kit (Cell Signaling Technology) was used

with IgG (Cell signaling Technology) and CIC (Acris) antibodies per the manufactures protocol.

ETV4 PCR primers were previously described (Okimoto et al., Nature Genetics 2016). The ETV4 primer sequences were as follows:

ETV4_Foward 5'-CGCATCAGACCCAAGACCGTGG-3'

ETV4_Reverse 5'-CCGGAGAGTCGTCCGGCCTGG-3'

CCNE1 PCR primers were designed to flank a tandem TGAATGAA/TGAATGAA sequence from positions -914 to -898 in the CCNE1 promoter. The primer sequences were as follows:

CCNE1_1F CGTCTCGGCCTCCCACAATGCTGGG and CCNE1_1R CGCGCCTGTGCCTTGGCCTAGAACC.

Chromatin immunoprecipitation – RNA-Seq (ChIPseq) analysis

CIC-DUX4 immunoprecipitation was performed using NCC_CDS_X1 cells. SimpleCHIP Enzymatic Chromatin IP Kit (Cell Signaling Technology) was used with IgG (Cell signaling Technology) and CIC (Acris) antibodies per the manufactures protocol. Paired-end 150bp (PE150) sequencing on a HiSeq platform was subsequently performed. ChIP-Seq peak calls were identified through Mode-based Analysis of ChIP-Seq (MACS).

Luciferase promoter assay. 293T cells were obtained from ATCC. Cells were grown in Dulbecco's modified Eagle Medium (DMEM), supplemented with 10% FBS, 100 IU/ml penicillin and 100ug/ml streptomycin in a 5% CO₂ atmosphere.

Cells were split into a 96 well plate to achieve 50% confluence the day of transfection. LightSwitch luciferase assay system (SwitchGear Genomics S720355) was used per the manufactures protocol. Briefly, a mixture containing FuGENE 6 transfection reagent, 50ng Luciferase GoClone *CCNE1* promoter (#S720355) plasmid DNA, 50ng of either control (empty) vector or CIC-DUX4 or wild-type CIC was added to each well. All transfections were performed in quintuplicate.

Western blot analysis. All immunoblots represent at least two independent experiments. Adherent cells were washed and lysed with RIPA buffer supplemented with proteinase and phosphatase inhibitors. Proteins were separated by SDS-PAGE, transferred to Nitrocellulose membranes, and blotted with antibodies recognizing: CIC (Acris/Origene AP50924PU-N), GFP (Cell Signaling #2956), HSP90 (Cell Signaling #4877), ETV4 (Lifespan LS-B1527), CCNE1 (Cell Signaling #20808), PARP (Cell Signaling #9532), Phosphor-RB (Cell Signaling), Actin (Sigma Clone AC-74), HA-tag (Cell Signaling #2367).

Real-Time Quantitative Polymerase Chain Reaction (RT-Q-PCR)

Isolation and purification of RNA was performed using RNeasy Mini Kit (Qiagen). 500 ng of total RNA was used in a reverse transcriptase reaction with the SuperScript III first-strand synthesis system (Invitrogen). Quantitative PCR included four replicates per cDNA sample. Human (CDK1, CDK2, CDK7, CDK9 CCNE1, CCNE2, ETV1, ETV4, ETV5, GAPDH, and TBP) and mouse (CCNE1, CCNE2, and GAPDH) were amplified with Taqman gene expression assays (Applied Biosystems). Expression data was acquired using an ABI Prism 7900HT

Sequence Detection System (Applied Biosystems). Expression of each target was calculated using the $2^{-\Delta\Delta Ct}$ method and expressed as a relative mRNA expression.

Transwell migration and invasion assays. RPMI with 10% FBS was added to the bottom well of a trans-well chamber. 2.5x10⁴ cells resuspended in serum free media was then added to the top 8 μM pore matrigel coated (invasion) or non-coated (migration) trans-well insert (BD Biosciences). After 20 hours, non-invading cells on the apical side of inserts were scraped off and the trans-well membrane was fixed in methanol for 15 minutes and stained with Crystal Violet for 30 minutes. The basolateral surface of the membrane was visualized with a Zeiss Axioplan II immunofluorescent microscope at 10X. Each trans-well insert was imaged in five distinct regions at 10X and performed in triplicate. % invasion was calculated by dividing the mean # of cells invading through Matrigel membrane / mean # of cells migrating through control insert.

Xenograft tumors. Subcutaneous xenografts were explanted on day 4 of treatment. Tumor explants were immediately immersed in liquid nitrogen and stored at -80 degrees. Tumors were disrupted with a mortar and pestle, followed by sonication in RIPA buffer supplemented with proteinase and phosphatase inhibitors. Proteins were separated as above. Antibodies to PARP and phosphor-RB were both from Cell Signaling.

Establishment of a CIC responsive gene set and identification of CIC-DUX4 target genes. A publicly curated Affymetrix mRNA dataset (GSE60740) of 14

CIC-DUX4 tumors, 7 EWSR1-NFATc2 tumors, and a CIC-DUX4 expressing cell line (IB120) expressing either shRNA's targeting CIC-DUX4 or control was used to generate a list of CIC-DUX4 responsive genes. Notably, the entire dataset was profiled on the same Affymetrix Human Genome U133 Plus 2.0 array, enabling a direct comparison between tumor types. We first independently compared IB120 cells expressing either EV control to each individual shRNA targeting the CIC-DUX4 fusion (shCIC-DUX4a and shCICDUX4b). Using logFC<-2 and FDR<0.05, we identified 409 (shCIC-DUX4a) and 205 (shCIC-DUX4b) downregulated genes, respectively. We then generated a shared gene list (N = 165) of downregulated genes that we referred to as "CIC-DUX4 responsive genes". We then used the CIC-DUX4 responsive gene set to perform functional clustering with Database for Annotation, Visualization, and Integrated Discovery (DAVID). We performed a similar analysis using logFC>2 and FDR<0.05 to identify 286 (shClC-DUX4a) and 168 (shClC-DUX4b) upregulated genes, respectively. There were 105 upregulated genes that were shared between these two datasets.

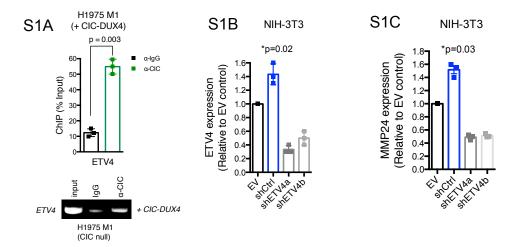
Using the CIC-DUX4 responsive gene set, we generated a gene expression heat map comparing: 1) IB120 cells expressing control vector and; 2) the two independent shRNAs targeting CIC-DUX4; 3) the 14 CIC-DUX4 patient derived tumors and; 4) the 7 EWSR1-NFATc2 tumors. Hierarchical clustering was performed using the differentially expressed CIC-DUX4 responsive gene set. We performed a similar hierarchical comparison of PAX3-FOXO1 positive cell lines (RH30) to CIC-DUX4 positive NCC_CDS_X1 cells as documented above. The PAX3-FOXO1 (RH30) and CIC-DUX4 (NCC_CDS_X1) cells were sequenced on the same RNAseq platform, enabling a direct comparison between the gene sets.

To identify putative CIC-DUX4 target genes, we surveyed all 165 CIC responsive genes for the CIC-binding motifs (TG/CAATGA/GA) within -2000bp and +150bp of the transcriptional start site. 43 of the 165 genes contained the CIC-binding motif. Human promoter sequences were downloaded from eukaryotic promoter database (http://epd.vital-it.ch/).

Cell cycle analysis. To determine the effect of CIC-DUX4 expression on cell cycle, NIH-3T3 cell lines were cultured to ~70% confluence and transfected with CIC-DUX4 or a GFP control vector for 48 hours. Cells were trypsinized and fixed in ice cold ethanol for 10 minutes and subsequently stained with propidium iodide (PI) solution (Sigma Aldrich) at room temperature for 15 minutes. Cells were analyzed on a BD LSRII flow cytometer.

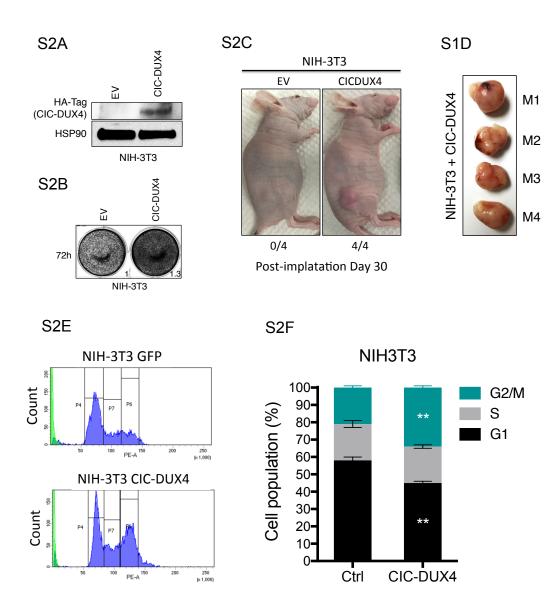
Statistical analysis. Experimental data are presented as mean +/- SEM. P-values derived for all in-vitro experiments were calculated using two-tailed Student's t test or one-way ANOVA. A P-value <0.05 was considered statistically significant.

Study approval. For tumor xenograft studies, including orthotopic and subcutaneous models, specific pathogen-free conditions and facilities were approved by the American Association for Accreditation of Laboratory Animal Care. Surgical procedures were reviewed and approved by the UCSF Institutional Animal Care and Use Committee (IACUC), protocol #AN107889-03A.



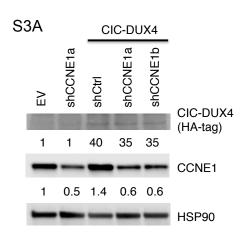
Supplemental Figure 1. CIC-DUX4 promotes invasion and metastasis through ETV4

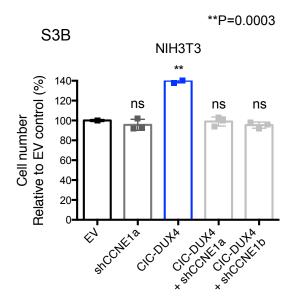
A) ChIP-PCR from H1975 M1 (CIC wild-type null) cells reconstituted with CIC-DUX4 showing CIC-DUX4 occupancy on the *ETV4* promoter. ETV4 (B) and MMP24 (C) protein expression in NIH-3T3 cells expressing either EV or CIC-DUX4 with shCtrl, shETV4a, or shETV4b. Performed in triplicate and quantified using Image J software.

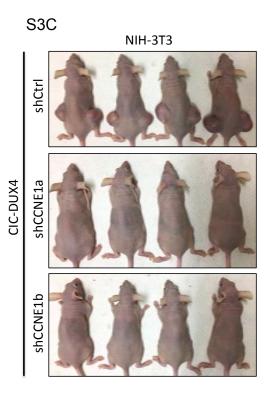


Supplemental Figure 2. CIC-DUX4 regulates cell-cycle progression and tumor growth

A) Immunoblot of CIC-DUX4 (HA-tag) and HSP90 in NIH-3T3 cells. B) Crystal violet assay comparing NIH-3T3 cells expressing either EV control or CIC-DUX4. C) Subcutaneously implanted NIH-3T3 cells expressing either EV control (n=4) or CIC-DUX4 (n=4). D) Tumor explants from mice in S2C. E) Cell-cycle profiles of NIH-3T3 cells expressing GFP control (top) or CIC-DUX4 (bottom). F) Cell-cycle distribution of NIH-3T3 cells expressing either EV control or CIC-DUX4 alone. Performed in triplicate. **p-value = <0.005. Error bars represent SEM.

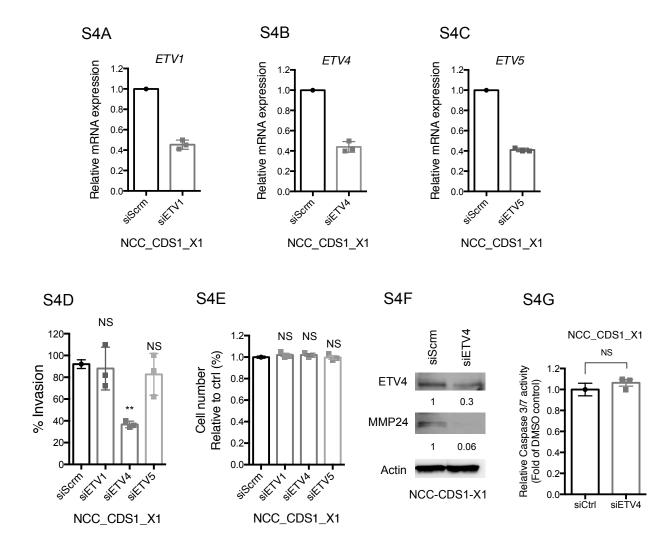






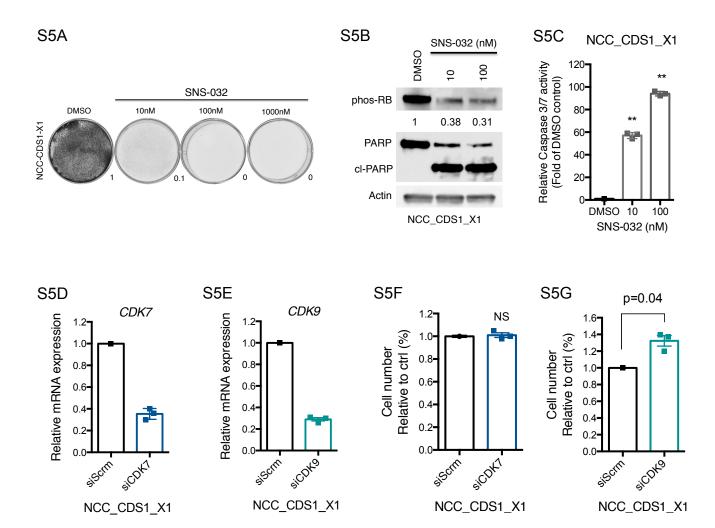
Supplemental Figure 3. CCNE1 inhibition decreases tumor growth in CIC-DUX4 expressing cells

A) Immunoblot of CIC-DUX4 (HA-Tag), CCNE1, and HSP90 in NIH-3T3 cells. B) Relative cell number of NIH-3T3 cells expressing either EV, shCCNE1a, CIC-DUX4 with or without shCCNE1a or shCCNE1b. **p-value = 0.0003. C) Subcutaneously implanted NIH-3T3 cells expressing CIC-DUX4 and either shCtrl, shCCNE1a, or shCCNE1b.



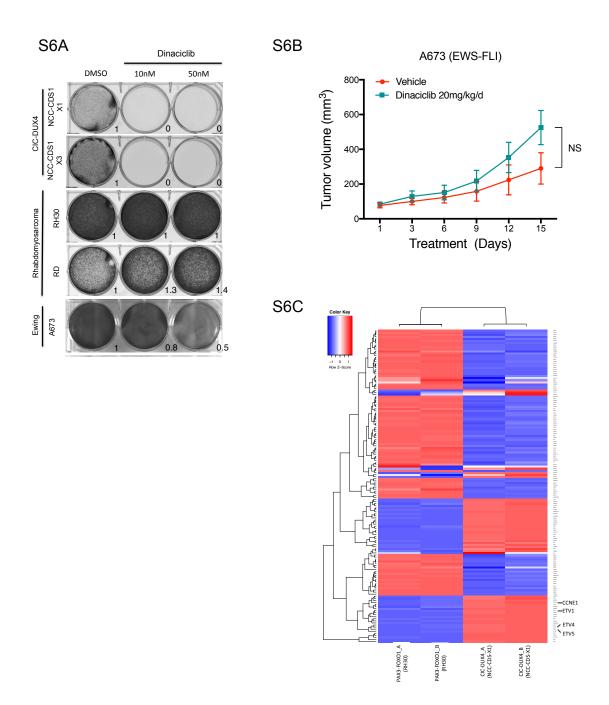
Supplement Figure 4. ETV4, but not ETV1 or ETV5 controls CIC-DUX4 mediated invasion

Relative *ETV1* (A), *ETV4* (B), and *ETV5* (C) mRNA expression in NCC_CDS1_X1 cells expressing either siETV1, siETV4, and siETV5 compared to siScrm. Performed in triplicate. Error bars represent SEM. D) Transwell invasion assay comparing NCC_CDS1_X1 cells expressing either siScrm, siETV1, siETV4, and siETV5. Performed in triplicate. Error bars represent SEM. E). Relative cell number of NCC_CDS1_X1 cells expressing either siScrm, siETV1, siETV4, and siETV5. Performed in triplicate. Error bars represent SEM. F) Immunoblot of ETV4 and MMP24 from NCC_CDS1_X1 cells expressing either siScrm control or siETV4. G) Relative caspase 3/7 activity in NCC_CDS1_X1 cells expressing either siScrm control or siETV4. Performed in triplicate. Error bars represent SEM.



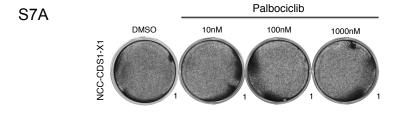
Supplemental Figure 5. Pharmacologic inhibition of CDK2 with SNS-032 induces apoptosis in CIC-DUX4 expressing cells

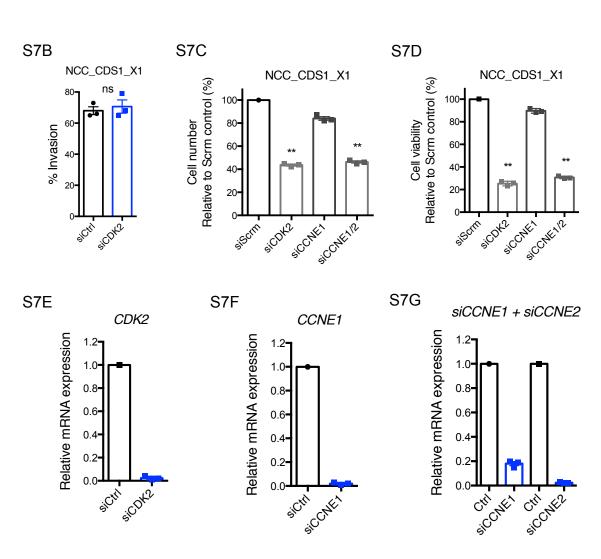
A) 72 hour crystal violet assay of NCC_CDS1_X1 cells treated with SNS-032. B) immunoblot of phosphorylated-Rb, PARP, and Actin from NCC_CDS_X1 cells treated with SNS-032 or DMSO. C) Relative caspase 3/7 activity in NCC_CDS1_X1 cells treated with SNS-032 or DMSO. **p-value < 0.0001, one-way ANOVA. Relative CDK7 (D) and CDK9 (E) mRNA expression in NCC_CDS1_X1 cells expressing either siScrm control, siCDK7, or siCDK9 respectively. Performed in triplicate. Error bars represent SEM. F) Relative cell number of NCC_CDS_X1 cells expressing either siScrm or siCDK7. Performed in triplicate. Error bars represent SEM. G) Relative cell number of NCC_CDS1_X1 cells expressing either siScrm or siCDK9. Performed in triplicate. Error bars represent SEM. G) Relative cell number of NCC_CDS1_X1 cells expressing either siScrm or siCDK9. Performed in triplicate. Error bars represent SEM. P-values calculated by Student's T-test.



Supplemental Figure 6. The CCNE-CDK2 complex is a specific therapeutic target in CIC-DUX4 tumors

A) 72 hour crystal violet assay of CIC-DUX4 (NCC_CDS1_X1 and NCC_CDS1_X3), rhabdomyosarcoma (RD and RH30), Ewing sarcoma (A673) cells treated with vehicle or dinaciclib. B) Subcutaneously implanted Ewing sarcoma (A673) cells treated with either vehicle (n=6) or dinaciclib (n=6). Error bars represent SEM. C) Heatmap comparing 165 CIC-DUX4 activated genes identified in CIC-DUX4 expressing NCC-CDS1-X1 cells vs PAX3-FOXO1 containing RH30 cells. CCNE1, ETV1, ETV4, and ETV5 are magnified.

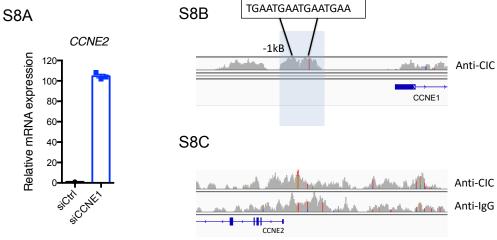


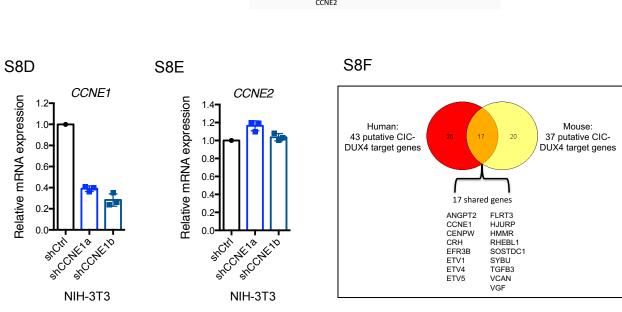


Supplemental Figure 7. Genetic inhibition of the CCNE-CDK2 complex decreases CIC-DUX4 tumor growth

A) Five day crystal violet assay of NCC_CDS1_X1 cells treated with palbociclib.

B) Transwell invasion assay comparing CIC-DUX4 expressing NCC_CDS1_X1 cells with either siCtrl or siCDK2. Error bars represent SEM. C) Relative cell number of NCC_CDS1_X1 cells following knockdown of CDK2, CCNE1, and combination CCNE1 and CCNE2 compared to scramble control. **p-value = 0.0001, one-way ANOVA. Error bars represent SEM. D) Relative cell viability (cell titer glo assay) of NCC_CDS1_X1 cells following knockdown of CDK2, CCNE1, and combination CCNE1 and CCNE2 compared to scramble control. **p-value = 0.0001, one-way ANOVA. Error bars represent SEM. E) Relative mRNA expression following CDK2 (E), CCNE1 (F), or dual CCNE1 and CCNE2 (G) knockdown compared to scramble control. performed in triplicate. Error bars represent SEM.





Supplemental Figure 8. CCNE1 is a conserved CIC-DUX4 target gene

A) Relative *CCNE2* mRNA expression following *CCNE1* knockdown compared to scramble control in NCC_CDS1_X1 cells. B) CIC-DUX4 binding sites and ChIP-Seq peaks on the *CCNE1* promoter in NCC_CDS1_X1 cells. C) ChIP-Seq analysis of the CCNE2 promoter region comparing anti-CIC and anti-IgG immunoprecipitations. Relative *CCNE1* (D) and *CCNE2* (E) mRNA expression following *CCNE1* knockdown compared to scramble control in CIC-DUX4 expressing NIH-3T3 cells. Performed in triplicate. Error bars represent SEM. F) Venn diagram comparing human (n=43) and mouse (n=37) putative CIC-DUX4 targets demonstrating 17 shared genes.

	regulated genes		
GeneSymbol ACVRL1	ID.x 94 at	adj.P.Val.x 0.007062	
ADAMTS9	56999_at	0.007062	
AGR2	10551 at	0.04047	
ANGPT2	285 at	0.012833	
APOBEC3B	9582_at	0.012637	-4.44
ATAD2	29028_at	0.004162	-3.75
AURKA	6790_at	0.004515	
AURKB	9212_at	0.007277	
BIRC5	332_at	0.008102	
BLM BMP4	641_at	0.003109 0.023837	
BPI BPI	652_at 671 at	0.023837	-2.33 -3.16
BTBD11	121551 at	0.00563	
BUB1B	701 at	0.010978	
CALB2	794_at	0.012137	
CCDC3	83643_at	0.012416	-2.26
CCNE1	898_at	0.003636	
CCNE2	9134_at	0.005342	
CDC20	991_at	0.005393	
CDC45 CDC6	8318_at 990_at	0.011462 0.004857	-3.58 -4.91
CDC7	8317 at	0.004837	
CDCA5	113130 at	0.000338	
CDCA7	83879_at	0.010166	
CDCA8	55143_at	0.001873	
CDH4	1002_at	0.034988	
CDK1	983_at	0.003935	
CDT1	81620_at	0.007726	
CENPE	1062_at	0.011145	
CENPK	64105_at	0.006043	
CENPM	79019_at	0.00155	
CENPU	79682_at 387103 at	0.004162 0.012751	-4.18
CEP152	22995_at	0.012751	
CHAF1A	10036 at	0.003652	
CHTF18	63922_at	0.00155	
CIT	11113_at	0.002885	
CKAP2L	150468_at	0.008394	-4.29
COLEC11	78989_at	0.008331	-3.57
CRH	1392_at	0.011093	
CYP2S1	29785_at	0.010176	
DDIAS	220042_at	0.007279	
DEPDC1B DIO3	55789_at 1735 at	0.011113 0.004162	
DLGAP5	9787 at	0.004162	
DTL	51514_at	0.003109	
E2F8	79733_at	0.005526	
EFR3B	22979_at	0.008838	-2.94
ELOVL6	79071_at	0.005324	-3.2
ENPP2	5168_at	0.004882	
ETV1	2115_at	0.018832	
ETV4	2118_at	0.021186	
ETV5	2119_at	0.005048	
EZH2	9156_at 2146_at	0.011245 0.031747	
FAM64A	54478_at	0.031747	
FAM83D	81610 at	0.002189	
FANCI	55215_at	0.008394	
FEN1	2237_at	0.007656	
FGFBP3	143282_at	0.006618	
FIGNL1	63979_at	0.004486	
FLRT3	23767_at	0.003727	
FOS	2353_at	0.00463	_
FOXM1	2305_at	0.011748	
GALNT16 GINS2	57452_at 51659_at	0.005088 0.007521	
GLCCI1	113263 at	0.007321	
GTSE1	51512 at	0.006618	
HAUS8	93323_at	0.013919	
HCRTR2	3062_at	0.004162	
HELLS	3070_at	0.004486	
HEY1	23462_at	0.003927	-4.1
HJURP	55355_at	0.025418	_
HMMR	3161_at	0.003877	_
ID1	3397_at	0.00472	
ID2	3398_at	0.002189	
IL18R1	8809_at	0.008314	
IRX1	79192_at	0.00363	
KIAA0101 KIF11	9768_at 3832 at	0.003356 0.004515	_
KIF11 KIF14	9928 at	0.004515	
		1 0.00+003	7.44
KIF15	56992_at	0.007378	-4.13

KIF2OA 10112_at 0.009833 -5.66 KIF2C 11004_at 0.005093 -4.16 KIFAA 24137_at 0.009833 -5.46 KIFC1 3833_at 0.009228 -3.94 LBH 81606_at 0.040084 -2.48 LINCO0473 90632_at 0.001154 -4.96 LINCO0911 100996280_at 0.009166 -2.51 LMNB1 4001_at 0.00463 -4.76 LOC100506718 100506718_at 0.003575 -3.92 LPCAT1 79888_at 0.00463 -4.76 MAFB 9935_at 0.003109 -2.17 MAFB 9935_at 0.003109 -4.5 MCM1 55388_at 0.003109 -4.5 MCM2 4171_at 0.01357 -3.68 MCM3 4172_at 0.004162 -2.6 MCM7 4176_at 0.011905 -2.83 McM7 4176_at 0.01507 -2.5 MFSD2A 84879_at </th <th>GanaSymbol</th> <th>ID.x</th> <th>adi B Val v</th> <th>logEC v</th>	GanaSymbol	ID.x	adi B Val v	logEC v
KIF2C 11004_at 0.005093 -4.16 KIFAA 24137_at 0.009833 -5.44 KIFC1 3833_at 0.009228 -3.99 LBH 81606_at 0.040084 -2.48 LHX1 3975_at 0.028595 -2.44 LINC00911 100996280_at 0.001154 -4.96 LINC00911 100996280_at 0.00463 -4.74 LOC100506718 40004575 -3.02 LEPCAT1 79888_at 0.004857 -3.02 LRRC1 55227_at 0.003109 -2.13 MAD2L1 4085_at 0.003144 -3.87 MAFB 9935_at 0.003784 -2.75 MCM10 55388_at 0.003784 -2.75 MCM11 55388_at 0.001507 -2.81 MCM3 4172_at 0.010507 -2.81 MCM5 4174_at 0.010507 -2.81 MCM5 4172_at 0.010507 -2.81 MCM5 4172_at 0.	GeneSymbol KIF20A			_
KIF4A 24137_at 0.009833 -5.44 KIFC1 3833_at 0.009228 -3.94 LBH 81606_at 0.040084 -2.44 LHX1 3975_at 0.028595 -2.62 LINC00911 100996280_at 0.009146 -2.55 LMNB1 4001_at 0.00463 -4.74 LOC100506718 100506718_at 0.003575 -3.92 LPCAT1 79888_at 0.003199 -2.13 MADAL1 4085_at 0.003149 -2.53 MAFB 9935_at 0.003199 -4.5 MAFB 9935_at 0.003199 -4.5 MCM1 4171_at 0.01507 -2.83 MCM10 55388_at 0.003109 -4.5 MCM2 4171_at 0.01507 -2.83 MCM3 4172_at 0.001507 -2.83 MCM5 4174_at 0.010507 -2.83 MCM7 4176_at 0.011505 -2.83 MYBD2 4606_at				
LBH 81606_at	KIF4A		0.009833	-5.44
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LINCO0473 90632_at				-2.48
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VGLL2 245806_at 0.012671 -2.88 ZNF804A 91752_at 0.010166 -3.97			0.02702	-2.02
_		245806_at		
ZWINT 11130_at 0.004826 -4.51				
	ZWINT	11130_at	0.004826	-4.51

ABI3BP ADAM12 ADAM12 ADAM175 AGO3 AGO3 AGO3 AGO4 ARNT2 ATF981 ATF981 ATF981 ATF986 C15orf48 C2CD2 C3AR1 C3orf52 CA8 CCARD6 CCD274 CEMIP CEMIP CEMIP CEMIP CUDM1 COLGA1 COL	25890_at 8038_at 11174_at 1192669_at 316_at 10123_at 9915_at 5205_at 10079_at 1222525_at 84419_at 25966_at 719_at 7669_at 767_at 84674_at 29126_at 57214_at 29126_at 1277_at 11281_at 115908_at 115908_at 115908_at 115908_at 115908_at 115908_at 115908_at 115908_at 11591_at 22943_at 144595_at 1996_at 1998_at 129943_at 129943_at 129943_at 129943_at 129943_at 129943_at 12996_at 122946_at 12296_at	0.011435 0.004483 0.002189 0.020917 0.0020917 0.002004 0.00155 0.034627 0.01325 0.00366 0.001325 0.007278 0.00294 0.010507 0.009144 0.000314 0.0003144 0.00321 0.00786 0.004515 0.00885 0.004515 0.00865 0.004515 0.003356 0.004535 0.00356	3.717.3 3.622.3 3.080.3 2.1.1.3 3.622.2 2.121.3 3.624.3 3.624.3 3.644.5 5.515.3 2.87.3 2.87.3 2.87.3 3.64.3 3.72.3 3.72.3 3.83.3 3.83.3 3.83.3 3.83.3 3.64.3 3.64.3 3.64.3 3.64.3 3.72.3
ADAMTS6 AGO3 AGO3 AGO3 AGO3 AGO3 AGO3 AGN1 ARL4C ARN12 ATP981 ATP981 ATP981 ATP981 C15orf48 C2CD2 C3AR1 C3orf52 CA8 CCARD6 CCD274 CEEMIP2 CLDN1 COLGA1 COLGA	11174_at 192669_at 316_at 10123_at 9915_at 5205_at 10079_at 122525_at 84419_at 25966_at 719_at 7669_at 767_at 84674_at 29126_at 29126_at 1277_at 1281_at 1277_at 1281_at 1359_at 115908_at 115908_at 1591_at 2943_at 344595_at 1845_at 1996_at 125943_at 22946_at 12596_at 12596_at	0.002189 0.020917 0.002004 0.00155 0.034627 0.010206 0.013976 0.001325 0.007866 0.001325 0.00787 0.00927 0.00927 0.00927 0.00946 0.005144 0.000776 0.00946 0.005144 0.000776 0.00946 0.005144 0.000776 0.00946 0.005144 0.000736 0.004515 0.00325 0.0032 0.004515 0.003356 0.014541 0.003356 0.014541 0.00463	3.088 2.1.1 3.088 6.022 2.121 3.622 2.331 3.644 5.5151 3.6.6 5.517 3.2.288 3.6.6 5.557 3.2.233 3.303 3.766 5.557 3.2.2.72 3.886 2.677 3.2.2.76
AOX1 ARL4C ARL4C ARL4C ARL4C ARNT2 ATP8B1 ATP9A C14orf28 C15orf48 C2CD2 C3AR1 C3orf52 CA8 CARD6 CD274 CEMIP2 CLDM1 COL1AD1 COL3A1 COL4C12 CD1AD1 COL4C12 CD1AD1 COL4C12 CPA3 CTHRC1 CVP24A1 DWR DUSP3 EDN1 EGR1 EU12 FGF1 FILIP11 FRMD6 FST GAPLINC GAS6 GBP1 GBP2 GDP15	316_at 10123_at 9915_at 19915_at 10079_at 122525_at 84419_at 25966_at 719_at 79669_at 79669_at 7967_at 84674_at 29126_at 57214_at 23670_at 1277_at 1281_at 81035_at 115908_at 115908_at 115908_at 11591_at 22943_at 344595_at 1845_at 1996_at 1998_at 12593_at	0.002004 0.00155 0.0134627 0.010206 0.0013976 0.0013976 0.001325 0.001294 0.001292 0.009272 0.009272 0.00940 0.005144 0.005144 0.0007378 0.002885 0.00328 0.00328 0.00328 0.00328 0.004515 0.003356 0.014541 0.00463 0.009119 0.0091325 0.00325	4.488.46.022.121.31.36.46.022.31.36.46.022.31.36.46.02.31.36.46.31.36.46.31.36.47.36
ARLAC ARNT2 ATPSB1 ATPSB1 ATPSB3 C14orf48 C2CD2 C3AR1 C3orf52 CA8 CARD6 C0274 CEMIP2 CUDN1 COLOL3A1 CO	10123_at 9915_at 5205_at 10079_at 122525_at 84419_at 25966_at 719_at 7669_at 767_at 84674_at 29126_at 29126_at 29126_at 1277_at 1281_at 1277_at 1281_at 1359_at 115908_at 115908_at 115908_at 115908_at 12918_at 2945_at 1259_at	0.00155 0.034627 0.010206 0.013976 0.013976 0.007866 0.007876 0.007876 0.009272 0.009272 0.00940 0.005144 0.000776 0.009444 0.003221 0.004515 0.00356 0.004515 0.003356 0.014541 0.003356 0.014541 0.004515 0.004515 0.004515 0.004515 0.00356	6.022 2.121 3.624 5.515 5.515 5.515 5.515 5.494 5.525 5.73 3.644 5.515 5.494 5.494 5.515 5.77 3.2.2 5.57 3.2.2 3.838 3.033 3.76 5.2.72 3.868 5.2.67 7.2.66 7
ATP8B1 ATP9A C14orf28 C15orf48 C2cD2 C3AR1 C3crf52 CA8 CARD6 CD274 CEMIP2 CLDM1 COL14D1 COL14D	9915. at 5205_at 10079_at 122525_at 84419_at 25966_at 719_at 79669_at 767_at 84674_at 29126_at 57214_at 23670_at 9076_at 1277_at 1281_at 1281_at 81035_at 1359_at 1359_at 1591_at 22943_at 1591_at 22943_at 1845_at 1996_at 1958_at 1958_at 1279_at 1289_at 1299_at 1299_at 1299_at 1299_at	0.034627 0.010206 0.007366 0.007376 0.007376 0.002994 0.005144 0.005144 0.000776 0.00947 0.00947 0.00321 0.00324 0.00324 0.00324 0.00325 0.00325 0.004515 0.003876 0.014541 0.004615 0.004615 0.004615 0.004615 0.004615 0.004615 0.004615 0.004615 0.004615 0.004615 0.004615 0.004615 0.004615 0.004615 0.004615 0.004615 0.004615 0.004615	2.122 2.313 3.662 2.877 3.6.65 2.877 3.223 3.722 3.322 3.323 3.323 3.642
ATP9A C14orf28 C14orf28 C14orf28 C14orf28 C15orf48 C2CO2 C3AR1 C3GAR1 C3GAR1 C3GAR1 C3GAR1 C3GAR1 C3GAR1 C3GAR1 CARD6 CD274 CEMIP CEMIP CEMIP CCULA1 COL1A1	10079_at 102525_at 84419_at 25966_at 719_at 79669_at 767_at 84674_at 29126_at 29126_at 29126_at 1277_at 1281_at 81035_at 1187_at 115908_at 11591_at 22943_at 344595_at 1845_at 1996_at 1996_at 1958_at 122946_at 11259_at 11259_at	0.013976 0.007866 0.007328 0.007278 0.002994 0.010507 0.009272 0.00946 0.005144 0.000776 0.00324 0.00324 0.00325 0.00325 0.00345 0.00325 0.00325 0.00326	2.31 3.64 5.51 2.87 3.66 2.31 2.08 2.01 5.49 5.57 3.22 3.23 3.83 3.03 3.76 2.72 3.86 2.67 2.72
C14oft28 C15oft48 C15oft48 C15oft48 C15oft48 C2CD2 C3AR1 C3oft52 CA8 CARD6 CCD274 CEMIP CEMIP2 CCLDN1 COL1A1 COL1A1 COL3A1 COL4C12 CPA3 CTHRC1 CVP24A1 DKK1 DUBR DUBR DUBP3 EDN1 EGR1 EGR1 ELL2 FGF1 FILIP11 FRMD6 FST GASP6 GBP1 GBP2 GDP15	122525_at 84419_at 25966_at 719_at 79669_at 767_at 84674_at 29126_at 57214_at 23670_at 9076_at 1277_at 1281_at 81035_at 1359_at 1359_at 1591_at 12943_at 344595_at 1591_at 22943_at 14845_at 1956_at 1958_at 122786_at 11259_at 11259_at	0.007866 0.001325 0.001325 0.002994 0.010507 0.00927 0.00944 0.000776 0.00932 0.00321 0.00323 0.004515 0.018761 0.00385 0.014541 0.00463 0.004	3.64 5.51 2.87 3.6 2.31 2.08 2.01 5.49 5.57 3.22 5.57 3.23 3.83 3.76 2.72 3.86 2.67 2.76 7.26
C2CD2 C3AR1 C3GAR1 C3GAR1 C3GAR1 C3GAR1 C3GAR1 C3GAR1 CARDG CD274 CEMIP CEMIP CEMIP CCUBA1 COLSA1 CO	25966_ at 719_ at 79669_ at 7767_ at 84674_ at 29126_ at 57214_ at 29126_ at 1277_ at 1281_ at 1359_ at 1359_ at 1359_ at 1359_ at 1359_ at 14598_ at 14598_ at 12948_ at 12948_ at 12948_ at 12594_ at 12594_ at 12594_ at 12594_ at 12594_ at 12596_ at 11259_ at 11259_ at 11259_ at 11259_ at	0.007278 0.002994 0.002997 0.00957 0.00946 0.005144 0.000776 0.00321 0.007378 0.00322 0.00325 0.00325 0.00325 0.00325 0.004515 0.004515 0.004615 0.004615 0.004615 0.004615 0.004615 0.004615 0.004615	2.87 3.6 2.31 2.08 2.01 5.49 6.45 3.72 5.57 3.23 3.83 3.03 3.76 2.72 2.76 7.26
C3AR1 C3Orf52 CA8 CARD CA8 CARD CABC CABC CABC CABC CABC CABC CABC CAB	719_at 79669_at 767_at 84674_at 29126_at 57214_at 23670_at 9076_at 1277_at 1281_at 1359_at 1359_at 1359_at 1359_at 1591_at 22943_at 344595_at 1845_at 1996_at 12936_at 12236_at 11259_at	0.002994 0.010507 0.009272 0.00946 0.005144 0.003276 0.007476 0.007378 0.002885 0.0032 0.004515 0.004515 0.018761 0.004515 0.00463 0.009119 0.0012052 0.004535 0.004535	3.6 2.31 2.08 2.01 5.49 6.45 3.72 5.57 3.22 3.23 3.83 3.03 3.76 2.72 2.76 2.76 7.26
CA8 CARD6 CCD274 CEMIP CEMIP CEMIP COL3A1 COL3A1 COL3A1 COL5A2 COL3A1 COL5C12 CPA3 CTHRC1 CYP2AA1 DWK1 DUBR DUSP3 EBN1 EGR1 ELL2 FGG1 FILIP1 FILIP1 FFFMD6 GAPLINC GAS6 GBP1 GBP2 GDP15	767_at 84674_at 84674_at 29126_at 57214_at 23670_at 9076_at 1277_at 1281_at 81035_at 1359_at 1359_at 1591_at 22943_at 1591_at 22943_at 1845_at 1958_at 1958_at 12736_at 11259_at 11258_at 11258_at	0.009272 0.00946 0.005144 0.000776 0.00976 0.009744 0.003221 0.007378 0.0012092 0.002885 0.0032 0.004515 0.018761 0.00453 0.014541 0.00463 0.009119 0.001356	2.08 2.01 5.49 6.45 3.72 5.57 3.23 3.83 3.03 3.76 2.76 2.67 2.76
CARDÓ CD274 CEMIP CEMIP2 CLIDNI COLIA1 COLSA1 COLEC12 CPA3 CTHRC1 CVP24A1 DKK1 DUBR DUBR EBN1 EGR1 EGR1 EILIP1 EILIP1 EILIP1 EILIP6 GASG GBP1 GBP2 GDP15	84674_at 29126_at 57214_at 23670_at 9076_at 1277_at 1281_at 81035_at 1359_at 115908_at 115908_at 129243_at 344595_at 1996_at 1998_at 22946_at 12298_at 12298_at 1996_at	0.00946 0.005144 0.005144 0.000776 0.009444 0.003221 0.001292 0.00328 0.004515 0.018761 0.00326 0.00356 0.00356 0.00356 0.00356 0.00356 0.00356	2.01 5.49 6.45 3.72 5.57 3.23 3.83 3.03 3.76 2.72 3.86 2.67 2.76
CD274 CD274 CEMIP CEMIP CLDNI COLSA1	29126_at 57214_at 23670_at 23670_at 9076_at 1277_at 1281_at 81035_at 1359_at 115908_at 11591_at 22943_at 344595_at 1845_at 1996_at 1958_at 12598_at 12593_at 12593_at 12593_at	0.005144 0.000776 0.009444 0.0003221 0.007378 0.012092 0.002885 0.0032 0.004515 0.004576 0.003356 0.014541 0.009919 0.0093356	5.49 6.45 3.72 5.57 3.23 3.83 3.03 3.76 2.72 3.86 2.67 2.76 7.26
CEMIP2 CLIN1 COL1A1 COL3A1 COL5A1 COL5C12 CPA3 CTHRC1 CYP24A1 DKK1 DUBR DUSP3 EDN1 EGR1 EGR1 EILIP1L FRMD6 FST GAPLINC GAS6 GBP1 GBP2 GDP15	23670_at 9076_at 1277_at 1281_at 81035_at 1359_at 115908_at 1591_at 22943_at 344595_at 1996_at 1998_at 122943_at 19106_at 1958_at 12236_at 11259_at 11259_at 11259_at 11259_at 11259_at 11259_at 1126_at 10468_at	0.009444 0.003221 0.007378 0.012092 0.002885 0.0032 0.004515 0.018761 0.003356 0.014541 0.00463 0.009119 0.001325	3.72 5.57 3.2 3.23 3.83 3.03 3.76 2.72 3.86 2.67 2.76
CLDN1 COL3A1 COL3A1 COL3A1 COL5A1 COL6C12 CPA3 CTHRC1 CYP2AA1 DUBR DUSP3 EDN1 EGR1 EIL12 FGF1 FILIP11 FRMD6 FST GAPLINC GAS6 GBP1 GBP2 GDP15	9076 at 1277 at 1281 at 1281 at 81035 at 1359 at 115908 at 1591 at 22943 at 344595 at 1845 at 1996 at 1958 at 22936 at 122936 at 122746 at 11259 at 11259 at 11268 at 10468 at 10468 at	0.003221 0.007378 0.012092 0.002885 0.0032 0.004515 0.018761 0.003356 0.014541 0.00463 0.009119 0.001325 0.003356	5.57 3.2 3.23 3.83 3.03 3.76 2.72 3.86 2.67 2.76
COLSA1 COLECT2 CPA3 CTHRC1 CYP24A1 DKK1 DUBR DUSP3 EEDN1 EGR1 EGR1 EIL12 FGF1 FILIP1L FRIMD6 FST GAPLINC GAS6 GBP1 GBP2 GDP15	1281_at 81035_at 1359_at 115908_at 1591_at 22943_at 344595_at 1845_at 1906_at 1998_at 22936_at 2246_at 11259_at 122786_at 10468_at	0.012092 0.002885 0.0032 0.004515 0.018761 0.003356 0.014541 0.00463 0.009119 0.001325 0.003356	3.23 3.83 3.03 3.76 2.72 3.86 2.67 2.76 7.26
COLEC12 CPA3 CTHRC1 CYP24A1 DKK1 DUSP3 EDN1 EEGR1 EUL2 FGF1 FILIP1L FRMD6 FST GAPLINC GASG GBP1 GBP2 GDP15	81035_at 1359_at 115908_at 1591_at 22943_at 344595_at 1966_at 1958_at 22936_at 2246_at 11259_at 122786_at 10468_at	0.002885 0.0032 0.004515 0.018761 0.003356 0.014541 0.00463 0.009119 0.001325 0.003356	3.83 3.03 3.76 2.72 3.86 2.67 2.76 7.26
CTHRC1 CYP24A1 DUBR DUSP3 EDN1 EGR1 EGR1 ELL2 FGF1 FILIP1L FRMD6 FST GAPLINC GAS6 GBP1 GBP2 GDP15	1359_at 115908_at 115908_at 1591_at 22943_at 344595_at 1845_at 1906_at 1958_at 22936_at 2246_at 11255_at 122786_at 10468_at	0.004515 0.018761 0.003356 0.014541 0.00463 0.009119 0.001325 0.003356	3.03 3.76 2.72 3.86 2.67 2.76 7.26
CYP24A1 DKK1 DUBR DUSP3 EDN1 EGR1 ELL2 FGF1 FILIP1L FRMMD6 FST GAPLINC GAS6 GBP1 GBP2 GDF15	1591_at 22943_at 344595_at 1845_at 1906_at 1958_at 22936_at 2246_at 11259_at 112786_at 10468_at	0.018761 0.003356 0.014541 0.00463 0.009119 0.001325 0.003356	2.72 3.86 2.67 2.76 7.26
DKK1 DUBR DUSP3 EDN1 EGR1 ELL2 FGF1 FILIP1L FFRMD6 FST GAPLINC GAS6 GBP1 GBP2 GDF15	22943_at 344595_at 1845_at 1906_at 1958_at 22936_at 2246_at 11259_at 122786_at 10468_at	0.003356 0.014541 0.00463 0.009119 0.001325 0.003356	3.86 2.67 2.76 7.26
DUSP3 EDN1 EGR1 ELL2 FGF1 FILIP1L FRMD6 FST GAPLINC GAS6 GBP1 GBP2 GDF15	1845_at 1906_at 1958_at 22936_at 2246_at 11259_at 122786_at 10468_at	0.00463 0.009119 0.001325 0.003356	2.76 7.26
EDN1 EGR1 ELL2 FGF1 FILIP1L FRMD6 FST GAPLINC GAS6 GBP1 GBP2 GDF15	1906_at 1958_at 22936_at 2246_at 11259_at 122786_at 10468_at	0.009119 0.001325 0.003356	7.26
FILI2 FGF1 FILIP1L FRMD6 FST GAPLINC GAS6 GBP1 GBP2 GDF15	1958_at 22936_at 2246_at 11259_at 122786_at 10468_at	0.003356	2.74
FGF1 FILIP1L FRMD6 FST GAPLINC GAS6 GBP1 GBP2 GDF15	2246_at 11259_at 122786_at 10468_at		
FILIP1L FRMD6 FST GAPLINC GAS6 GBP1 GBP2 GDF15	11259_at 122786_at 10468_at	0.010102	2.01
FST GAPLINC GAS6 GBP1 GBP2 GDF15	10468_at	0.003567	4.48
GAPLINC GAS6 GBP1 GBP2 GDF15		0.011341	2.62
GAS6 GBP1 GBP2 GDF15	100505592_at	0.016401	2.88 4.72
GBP2 GDF15	2621_at	0.001325	3.46
GDF15	2633_at 2634_at	0.005038 0.015941	3.14
	9518_at	0.003833	4.01
GLIPR1	11010_at	0.006676	2.8
GLS GLT8D2	2744_at 83468_at	0.006551	2.22
HHAT	55733_at	0.015729	2.72
HIST1H1C HIST1H4H	3006_at 8365_at	0.009715 0.01762	2.61
HMOX1	3162_at	0.002539	4.04
HOXC6 HTR2B	3223_at	0.011744	2.02
IGFBP3	3357_at 3486_at	0.001921	6.44 4.13
IGFBP5	3488_at	0.011744	3.68
IGFBP7 KCTD12	3490_at 115207_at	0.002885 0.002562	6.37 2.98
KRTAP2-3	730755_at	0.000776	7.95
LAMB3 LINC00460	3914_at 728192_at	0.028202 0.016475	3.73 4.54
LOC151760	151760_at	0.010473	2.14
LRRC17	10234_at	0.008883	4.18
LTBP2 LYPD6B	4053_at 130576_at	0.015508 0.003948	2.32 3.4
MAP3K7CL	56911_at	0.006045	5.04
C3HC4 MBNL1-AS1	57574_at 401093 at	0.003609 0.004162	3.91 3.5
MGLL	11343_at	0.022738	3.16
MMP3	4314_at	0.007666	3.63
MOK MOXD1	5891_at 26002_at	0.014633	3.1 3.95
MSTN	2660_at	0.004395	4.97
MYBL1 MYLK	4603_at 4638_at	0.006166 0.003425	2.15 2.85
MYO1E	4643_at	0.003423	3.22
MYOF	26509_at	0.007773	2.67
NABP1 NEDD4	64859_at 4734_at	0.005731 0.012185	3.21 2.45
NMRK1	54981_at	0.018801	3.34
NOG OLFML3	9241_at 56944_at	0.003786 0.026353	5.68
OPTN	10133_at	0.020333	2.45
OXTR	5021_at	0.004832	5.81
PALMD PLA2G4C	54873_at 8605_at	0.002189	2.35 4.86
PLAT	5327_at	0.0216	3.99
PLAU	5328_at	0.008102	5.58
POSTN PSG4	10631_at 5672_at	0.004316 0.017603	3.59
PSG5	5673_at	0.011842	4.25
PTPRJ RCAN1	5795_at 1827_at	0.004515 0.041172	2.59 3.44
RGS7	6000_at	0.004882	3.62
S100A2	6273_at	0.003567	2.44
SCG5 SERPINE1	6447_at 5054_at	0.002521 0.019986	3.41 4.8
SLC22A4	6583_at	0.001154	4.19
SULF1 SYTL2	23213_at 54843_at	0.008102 0.010628	3.37 2.77
TGFBI	7045_at	0.010628	4.2
TIPARP	25976_at	0.003356	2.76
TMEM154 TMEM200A	201799_at 114801_at	0.008612	3.03 4.91
TMEM40	55287_at	0.001154	5.42
	4982_at 7164_at	0.000776 0.004634	5.89 2.7
TNFRSF11B TPD52L1	7164_at 81029_at	0.004634	3.7

Table S3. Puta	ative CIC-DU	X4 target genes - human
GeneSymbol	ID	Description
ANGPT2	285_at	angiopoietin 2
BLM	641_at	Bloom syndrome, RecQ helicase-like
CCNE1	898_at	cyclin E1
CDC45	8318_at	cell division cycle 45
CENPE	1062_at	centromere protein E, 312kDa
CENPM	79019_at	centromere protein M
CENPW	387103_at	centromere protein W
CRH	1392_at	corticotropin releasing hormone
CYP2S1	29785_at	cytochrome P450, family 2, subfamily S, polypeptide 1
DLGAP5	9787_at	discs, large (Drosophila) homolog-associated protein 5
EFR3B	22979_at	EFR3 homolog B (S. cerevisiae)
ELOVL6	79071 at	ELOVL fatty acid elongase 6
ETV1	2115_at	ets variant 1
ETV4	2118_at	ets variant 4
ETV5	2119_at	ets variant 5
FAM83D	81610_at	family with sequence similarity 83, member D
FANCI	55215_at	Fanconi anemia, complementation group I
FGFBP3	 143282_at	fibroblast growth factor binding protein 3
FLRT3	23767_at	fibronectin leucine rich transmembrane protein 3
GLCCI1	113263_at	glucocorticoid induced transcript 1
GTSE1	51512_at	G-2 and S-phase expressed 1
HELLS	3070_at	helicase, lymphoid-specific
HJURP	55355_at	Holliday junction recognition protein
HMMR	3161_at	hyaluronan-mediated motility receptor (RHAMM)
KIF4A	24137_at	kinesin family member 4A
KIFC1	3833_at	kinesin family member C1
MAD2L1	4085_at	MAD2 mitotic arrest deficient-like 1 (yeast)
MCM10		minichromosome maintenance complex component 10
MCM7	4176_at	minichromosome maintenance complex component 7
NEIL3	55247_at	nei endonuclease VIII-like 3 (E. coli)
PKNOX2	63876_at	PBX/knotted 1 homeobox 2
POLQ	 10721_at	polymerase (DNA directed), theta
RAD51AP1	 10635_at	RAD51 associated protein 1
RHEBL1	 121268_at	Ras homolog enriched in brain like 1
RRM2	6241_at	ribonucleotide reductase M2
SOSTDC1	25928_at	sclerostin domain containing 1
SULT1E1	6783_at	sulfotransferase family 1E, estrogen-preferring, member 1
SYBU	55638_at	syntabulin (syntaxin-interacting)
TGFB3	7043_at	transforming growth factor, beta 3
TGFBR3	7049_at	transforming growth factor, beta receptor III
VCAN	 1462_at	versican
VGF	7425_at	VGF nerve growth factor inducible
ZWINT	 11130_at	ZW10 interactor, kinetochore protein

Table S4. Puta	ative CIC-DU	X4 target genes - mouse
GeneSymbol	ID	Description
ANGPT2	285_at	angiopoietin 2
ATAD2	29028_at	ATPase family, AAA domain containing 2
AURKB	9212_at	aurora kinase B
BTBD11	121551_at	BTB (POZ) domain containing 11
CCNE1	898_at	cyclin E1
CENPU	79682_at	MLF1 interacting protein
CENPW	387103_at	centromere protein W
CHAF1A	10036_at	chromatin assembly factor 1, subunit A (p150)
CIT	11113_at	citron (rho-interacting, serine/threonine kinase 21)
CKAP2L	150468_at	cytoskeleton associated protein 2-like
CRH	1392_at	corticotropin releasing hormone
DEPDC1B	55789_at	DEP domain containing 1B
EFR3B	22979_at	EFR3 homolog B (S. cerevisiae)
ETV1	2115_at	ets variant 1
ETV4	2118_at	ets variant 4
ETV5	2119_at	ets variant 5
FLRT3	23767_at	fibronectin leucine rich transmembrane protein 3
FOS	2353_at	FBJ murine osteosarcoma viral oncogene homolog
HJURP	55355_at	Holliday junction recognition protein
HMMR	3161_at	hyaluronan-mediated motility receptor (RHAMM)
IL18R1	8809_at	interleukin 18 receptor 1
KIF18B	146909_at	kinesin family member 18B
MCM5	4174_at	minichromosome maintenance complex component 5
MYH13	8735_at	myosin, heavy chain 13, skeletal muscle
NID2	22795_at	nidogen 2 (osteonidogen)
ORC6	23594_at	origin recognition complex, subunit 6
PRICKLE1	144165_at	prickle homolog 1 (Drosophila)
RHEBL1	121268_at	Ras homolog enriched in brain like 1
SCARA5	286133_at	scavenger receptor class A, member 5 (putative)
SHC4	399694_at	SHC (Src homology 2 domain containing) family, member 4
SOSTDC1	25928_at	sclerostin domain containing 1
SYBU	55638_at	syntabulin (syntaxin-interacting)
TESC	54997_at	tescalcin
TGFB3	7043_at	transforming growth factor, beta 3
TSPAN11	441631_at	tetraspanin 11
VCAN	1462_at	versican
VGF	7425_at	VGF nerve growth factor inducible