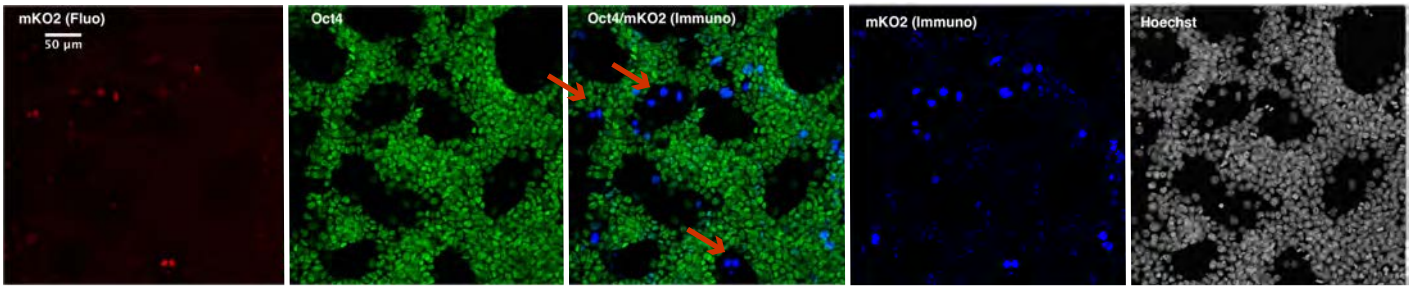
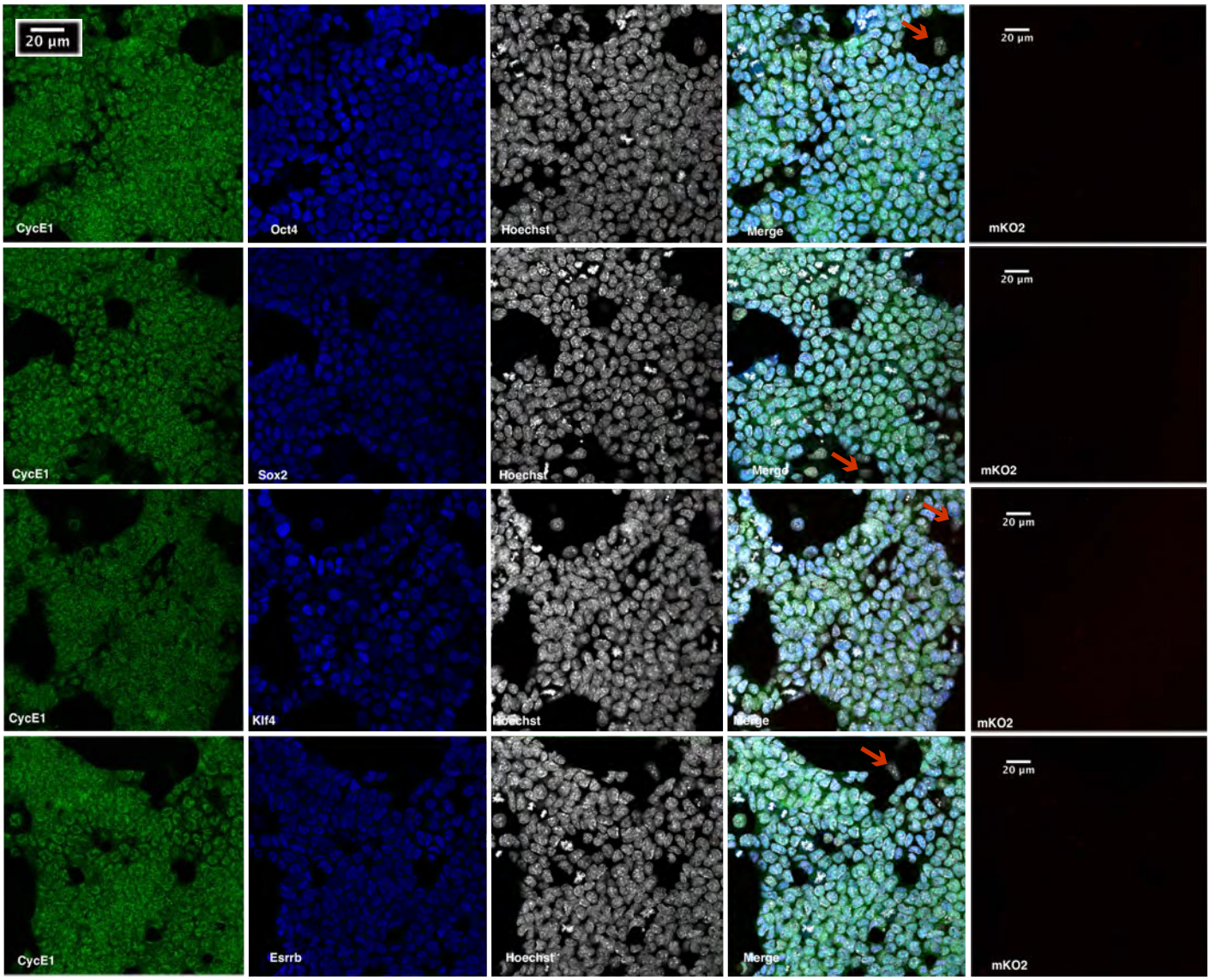
Supplementary Figure 1

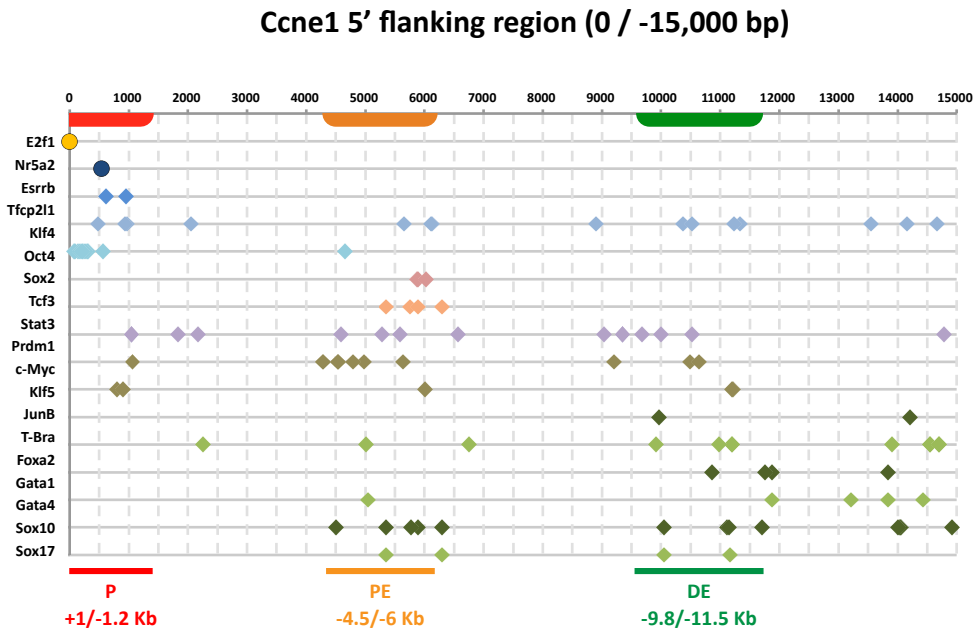
A



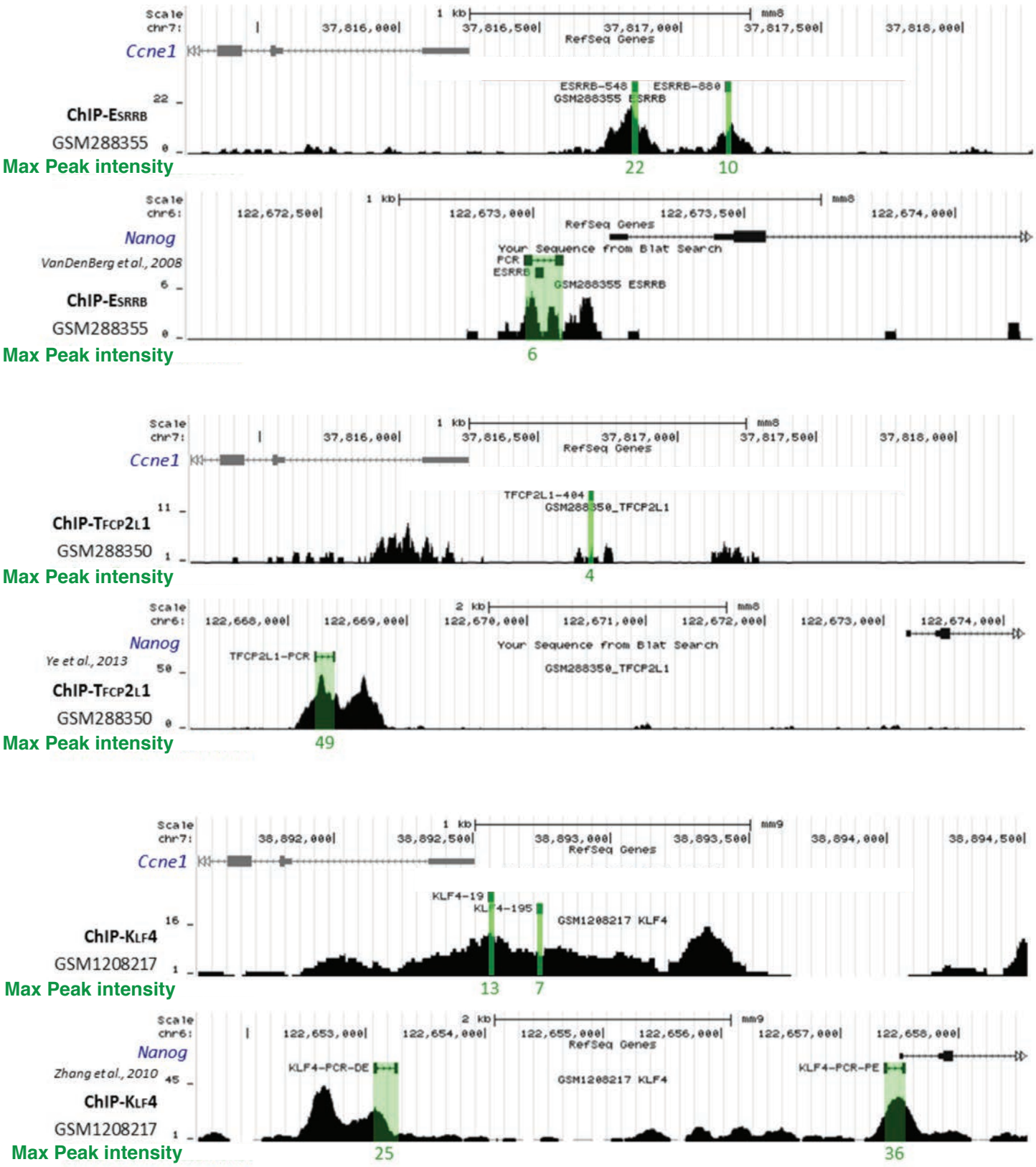
B



Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure 4

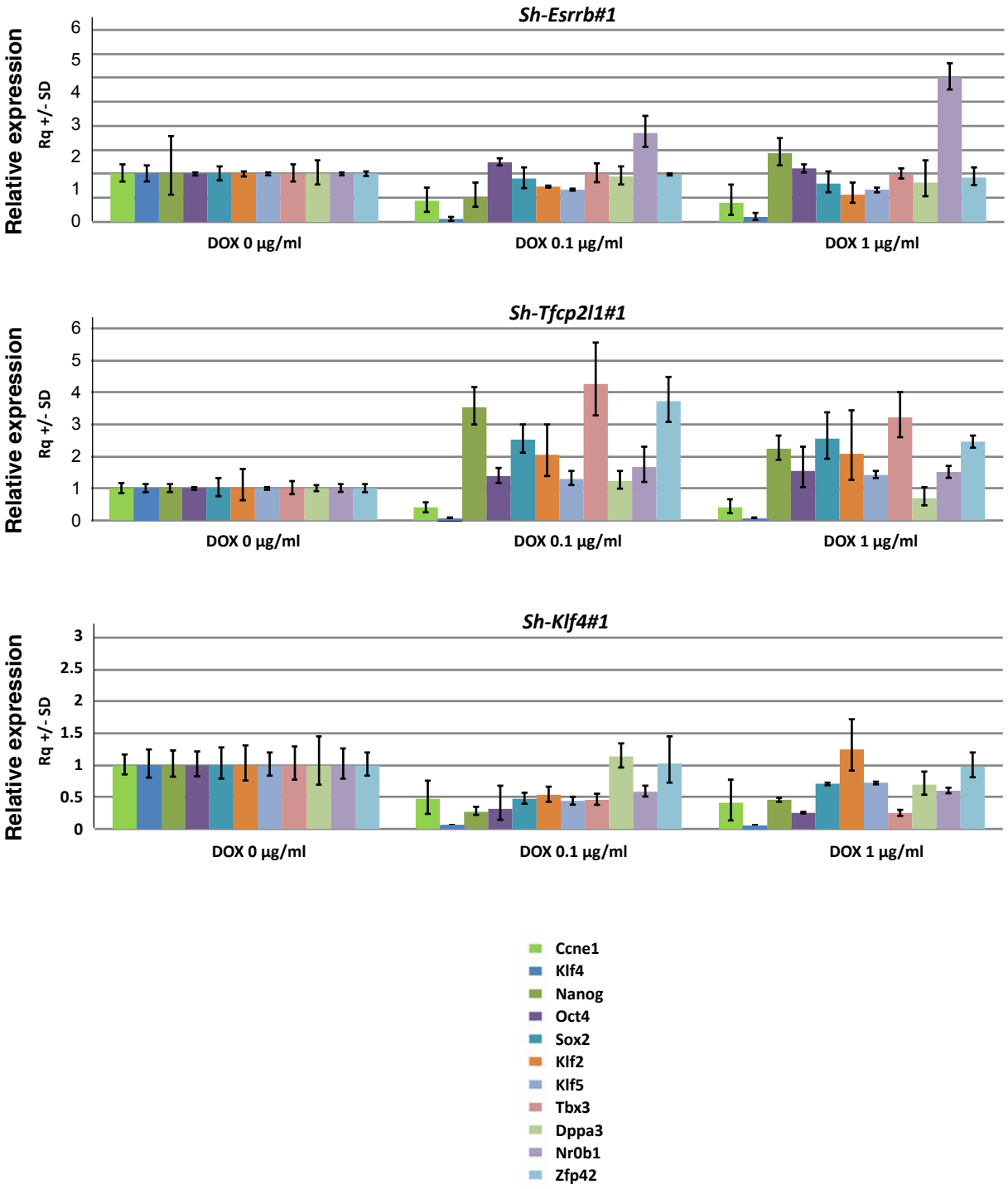


Table S1: PCR primers for qRT-PCR.

Target		Sequence (from 5' to 3')	Amplicon length
Actb	Forward	TTCTTTGCAGCTCCTTCGTTGCC	102 bp
NM_007393	Reverse	TTTGCACATGCCGGAGCCGTTG	
Ccna1	Forward	GGGTTCTTCTCTGGCTCCAA	181 bp
NM_007628	Reverse	AAAGAGTGTCAGCCTCCGGG	
Ccne1	Forward	TGGAGTTGATGCAGAAGGTC	208 bp
NM_007633	Reverse	ATGGCTTTCTTTGCTTGGGC	
Ccne2	Forward	ACTGATGGTGCTTGCAGTGA	220 bp
NM_001037134	Reverse	CGATGGCTAGAATGCACAGA	
Dppa3 (Stella)	Forward	AGGCTCGAAGGAAATGAGTTTG	124 bp
NM_139218	Reverse	TCCTAATTCTTCCCGATTTTCG	
E2f1	Forward	GCCCTTGACTATCACTTTGGTCTC	270 bp
NM_007891	Reverse	CCTTCCCATTTTGGTCTGCTC	
Esrrb	Forward	CTCGCCAACTCAGATTCGAT	187 bp
NM_011934	Reverse	AGAAGTGTTGCACGGCTTTG	
Gbx2	Forward	GGCACCTCCTAGATGTGGAC	161 bp
NM_010262	Reverse	AAAACACTGCAGCTGAGATCC	
Klf2	Forward	AGCCTATCTTGCCGTCCTTT	138 bp
NM_008452	Reverse	CCATGGAGAGGATGAAGTCC	
Klf4	Forward	CCAGCAAGTCAGCTTGTGAA	189 bp
NM_010637	Reverse	GGGCATGTTCAAGTTGGATT	
Klf5	Forward	GCCAGTTAATTCGCCAACTC	156 bp
NM_009769	Reverse	CCCGTATGAGTCCTCAGGTG	
Nanog	Forward	AAGCCATGCGCATTTTAGCACCC	127 bp
NM_028016	Reverse	AAGGAACCTGGCTTTGCCCTGAC	
C-Myc	Forward	AAGGAGAACGGTTCCTTCTGAC	106 bp
NM_010849	Reverse	GCTGAAGCTTACAGTCCCAAAG	
Nr0b1 (Dax1)	Forward	TATCTGAAAGGGACCGTGCT	92 bp
NM_007430	Reverse	ATCTGCTGGGTTCTCCACTG	
Nr5a2 (Lrh1)	Forward	TTGAGTGGGCCAGGAGTAGT	201 bp
NM_030676	Reverse	ACGCGACTTCTGTGTGTGAG	
Oct4 (Pou5f1)	Forward	ATGCAAATCGGAGACCCTGGTGC	147 bp
NM_013633	Reverse	AGCCCAAGCTGATTGGCGATGTG	
Sox2	Forward	AAGGGTTCTTGCTGGGTTTT	150 bp
NM_011443	Reverse	AGACCACGAAAACGGTCTTG	
Stat3	Forward	AAGACGAACTGCTTGCCTTG	191 bp
NM_213659	Reverse	AGAGAAGCCCTCACCTTGTT	
Tbx3	Forward	ATCTGCCAGTGCACTTTGTTAGATG	104 bp
NM_011535	Reverse	TGTTCTTCAGCCCCGACTTCCATAC	

Target		Sequence (from 5' to 3')	Amplicon length
Tfcp2l1	Forward	CCGCCCCTACAGTATGTGTT	104 bp
NM_023755	Reverse	AGCCGGATTTCATACGACTG	
Zfp42 (Rex1)	Forward	TGTGTGCAGAGTGTGGCAAAGC	142 bp
NM_009556	Reverse	TGGGTGCGCAAGTTGAAATCCAG	
Twf1 (Ptk9)	Forward	AATGAGCAACTGGTGGTTGG	136 bp
NM_008971	Reverse	GGGCATTCTGAGAGTCTAACCT	
mir 15a-5p / NR_029733	Forward	gcgcgcTAGCAGCACATA	65 bp
sno234 / AF357329	Forward	gcgcgcATTCGTCACTAC	142 bp
stem-loop for miRNA	Reverse	CCAGTGCAGGGTCCGAGGTA	-

Table S2: PCR primers for amplification of ChIP products.

Target		Sequence (from 5' to 3')	Amplicon length
Ccne1: binding site for ESRRB	Forward	CCTAACAGCAGCAGCCTGAA	136 bp
[-538/-548]	Reverse	ACTGTCCCTCCTGACTCGTC	
Ccne1: binding site for ESRRB	Forward	AAGCAAGCTCTGAGGCTCTG	125 bp
[-870/-880]	Reverse	ATGCACATGCCTCACAAACG	
Ccne1: binding site for KLF4	Forward	TCTAGCCCCACCCCTTTAGT	216 bp
[-9/-19]	Reverse	GCTTCGAGCGGGACATTTA	
Ccne1: binding site for KLF4	Forward	GATCTGCCCTGCTGACATTC	228 bp
[-185/-195]	Reverse	TAAAGGGGTGGGGCTAGATG	
Ccne1: binding site for TFCP2L1	Forward	ACGAGTCAGGAGGGACAGTG	188 bp
[-390/-404]	Reverse	AGCGCCTGAAGGATTCTGAG	
Ccne1 3'UTR	Forward	CTCGGGTGTTGTAGGTTGCT	112 bp
[+9358/+9469]	Reverse	CTGTTGGCTGACAGTGGAGA	
Nanog: binding site for ESRRB	Forward	GGATGCCCCCTAAGCTTTCC	95 bp
[-89/-97] (van den Berg et al., 2008)	Reverse	TAATCCCACCTGCAGGGTCC	
Nanog: binding site #12 for KLF4	Forward	TAGATCAGAGGATGCCCCCTAAGCTTTCCC	181 bp
[-137/+43] (Zhang et al., 2010)	Reverse	CTCCTACCCTACCCACCCCCTATTCTCCC	
Nanog: binding site for TFCP2L1	Forward	GACTGCTAACCACCCAGAGG	175 bp
[-4714/-4890] (Ye et al., 2013)	Reverse	TGAAAGATCCGAGCGAAGAG	

Van den Berg, D.L., Zhang, W., Yates, A., Engelen, E., Takacs, K., Bezstarosti, K., Demmers, J., Chambers, I., and Poot, R.A. (2008). Estrogen-related receptor beta interacts with Oct4 to positively regulate Nanog gene expression. Mol Cell Biol 28, 5986-5995.

Ye, S., Li, P., Tong, C., and Ying, Q.L. (2013). Embryonic stem cell self-renewal pathways converge on the transcription factor Tfcp2l1. EMBO J 32, 2548-2560.

Zhang, P., Andrianakos, R., Yang, Y., Liu, C., and Lu, W. (2010). Kruppel-like factor 4 (Klf4) prevents embryonic stem (ES) cell differentiation by regulating Nanog gene expression. J Biol Chem 285, 9180-9189.

Table S3: Nucleotide sequences (from 5' to 3') of the *Cyclin E* promoter regions I (P), II (PE) and III (DE), synthetized by GeneArt (Invitrogen), and of the *Esrrb*, *Klf4* and *Tfcp2l1* CDS, cloned for the overexpression.

Region I "Promoter" (P)
TCACCATTATGCTAGTCAGGACCTATGGGAAGGGCACACTCCACTTTGACTTCCAGAAGAGAGTCA
CTGGGAGCAGAGACAGGCTTACCCCGAGGAAGGTCCCCAGAGGTATTTAGACCCCGCCTTTCACAC
TTCTACAACTTGAGTACAGGTCTTTCTTTGCTAGCAGTCAATGTGCTCAAGGCATTCGTCTCAGTAG
CCTGTATGTTCCACAGACCTGGGTCAGTGTGGGTTTCTTTTCTCTCTTTCTTTCTTTCTTTCTTTCTTT
CTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTATATCATTTACTA
ACATAAGGGAAGTGACCCTTTTGGTCCAAGATACAGAAGGGGCAACGGGATAAGAAAACAGAGTG
AACAAGAGATTGGAAGAAACAAGTGCTTTGCCATAGTTTAACACTGGAGGGGACGTCCTGGGGAA
AGGTACGCCGGAGAGGAAGTGGTTACCAAAGACCTTCAAGTTTTCCGGAAGCACAAACAGCTGGA
ATGGGTCAGAAGAGAGTAAAGCAAGCTCTGAGGCTCTGGGGTGCGAAAGGGCACCGGATGCTGGA
TCCAGCAGCTCGGGCGGAGGGCTGAAGGTCAGGTCTGGGGTGGGTGAGGGTCACTTCACGTTTGTG
AGGCATGTGCATACTCTGAGGTTGATGAAAACACTTGGAGTAAAATTATAGGCTGGAGACTGCCTC
ACCTCATGGGGACCTAAGGGTCAGAGAGGCTTTCTGCAAACGGGTTGGGCCCATGTGTGCTAGAG
GCACAGAAATGTGCTTGGGTAGCCTAATGAATGAATGAATGGGTGGATGAATGGACCAGAAACAC
TGACAGGTTAAAGGACCTGCTGCTGGTCCACAGGAGACCTAACAGCAGCAGCCTGAATGCTGGTTC
CGGTCCCAGGAGCCACAAGCTGTTGTGACCTTGGGGACACCCACGCGCCGGACTCGGCCCGGAAC
TCTGCGTCTCAGGGGCGGGGAGGACGAGTCAGGAGGGACAGTGCGCGCGCGCGGGAGACCGGCG
GATGACGGGTTCTTAACTCCGGGCCCTCCCGTGCCTCACTCCAGTCAAGCCCGGCCGCCGATCATT
GCGATCTGCCCTGCTGACATTCCACTTGGGCGGCCCATGCCGCTCCTCCCGGCCCCGCACGCTCAG
AATCCTTCAGGCGCTCGCGCCAAGATTCTCCCGCGTCAGCGAGCCCGCCCCGCAGCCGCGCGCGCC
AGACGACTCTCCCGCGTCCCGCCCCGCGCAGGCCCCGCCTACCACGTCCGCACCCCGCCCCCGGCG
CGCAGGCCCTGACATCTAGCCCCACCCCTTTAGTGCATGCCACGCCCGTAAAAGAACACGCCCCCC
GGGAGGCCACGCCCCCACCAGAGCTCCTCGCTGGTCCGCGCGGCGACGGGGCGGGCCCCGGGCCT
GCGGCGGCCGCTGAGGGGCTCGCAGCCCTCGGGGCGGGGCGCGAGGGCG

Region II "Proximal Enhancer" (PE)
TTGCATCTAGGGATGCTGGCTTTCCATTTAGGGCAGGGACAGGAGGTTTTCCTTTGCAAACACATG
GACTAAAGTGGGAAATATAATTTGTAGTAAGAGGTCAAAGGTGGAGAGGCCCTCGGAACCCAGAA
CGGAGGGTGGAAGGAGGAGGGGGAAGCCTTGCCTTCACATGTGGAATAGCCTTTGTGTTTCTAACA
CCAGCAAAAGAATGTGCTGGGTACTGAACTCCACACGCCCAGCCTCCCGGAGCCTCCCAGGCCTCC
CCGGGCTTCCTATCACCTCCTGGAAAGGCATGCTGAAGCACACCCCTTTGTCCTCTATCCATTCATC
TATCCATTTATTTGCACAGACAAGCCAGGTTTCCAGAGTCTGGGCTGTGGTCTGTGCACACTCAGG
AGCGGACCTAGTTGTTTCTGGTCTCACCCCCTCCATGCTTTCTTCCTGTAATCTCAATCCTCCCCTGA
CCCTCCAGGCGCTGAGTCAGCTGGAATTCCTTCCTAGGTGGGGTTTCAAAGCCAGACAAGCAAAGA
GAACAGGTTGGTCCCTAAATTAGAAATAAAGATATGGGGCAAAATGACAATCATAACAATACTAA
GAGTAGTAATGAATAACGGTGATGATGATGATGGTGGTGGTGATGACGATGATAAAGATGCGAAA
CGGGGAGCTTCCTGCAGTTGTTGTGCACAGATGTGGGCTCAACTTTGCCAAATTATTCCATTGTCCC
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CCTGTCTGTGTGTAACTTCTGTTGGTTGCCAGGCCGATTGTAAGTGGATTCCAACGTGACAGATGAC
AGCGACTGAGGGATGTTAATAGACTTAGGCCTGGCACCCACAGAGGAATGTGTCCCTGGCTTCGCT
GACCTAGTGGGTGAGGACCGCTGCCCTGGGGATTCGGAGGCTTGCTGCAAAGCCTGACCAGTTGCT
CACTCTCTCACTCACTCATGACAACCATGATTTTCTGTGGCATAAGATAAGAAACCCAATCCCAAC
TAGCTAAGTCAATACTTGAAAATAATTGATTGGTTCCAGCATCCAGGAAGTTCCCAGTAATCCAGC
CTTAAGCTTGATTGGACACAGGGACTCAACAAATCGGAAACCTGCCTCCCAGCAAACACCCCCCCC
CCCCTCCACTCTGCTCTCCAGGAAGAGTTTGCCTCCAAAGCAGGTCAACTTATGTGGCAAGATGGC
CTCGTGGCTGCAAGCCCACTTCCAGTCAGCCTAGCAACTCCTGAGGAATGTCATTGGCTCCGCTTG
GGCCCCAGGCCTGTGCAGAAACCAATCACACAACCAGGAATGTGGTGCTCTGATTGGCCAAGGCC
CTGTCTCCCATCAAAGTGCCTCAGAGGGTGGTGCTTAGAGAAAAATGTTGATCTCTGACCAGAAGT
GAGAGCTGAGCCTCCTCCCTCAAGCCCCACCTCTGTGTTGCAGCTGT

Region III "Distal regulatory Element" (DE)

CCCAGAACCAGGTAAAAAGCTGGATGTGGCAGAGGCAGAGAGGTGAATTCTGGGGGTTCAATGGC
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CCAATGCAATACCAACAACAAGAGCAAGAGAAGAGGGGAAGGAGGGAAGGAAAGGGAAATGAG
AAGGAAGGAGGGAGGGAGGGAGGGAGAGAGGGAGGGAGGGAGGGAGGGAGGAAGAGACTGATA
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GCTCACAATGTAGACCAGGCTGGTCTCAAATTCACAGAGATCCACCAGAGATCCACCTGCCTCTGC
CCCTCAGGTGCTGGTGTTAAAGGCATTCACCACTAGGGCTGGCAGACAAGTCAATTGTTTTGTTTTG
GGTTTTTTGTTTGTTTTGTTTTGTTTTGTTTTGTTTTGTTTTTCGAGACAGGGTTT

***Esrrb*, transcript variant 1 (NM_011934)**

ATGGACGTGTCCGAACTCTGCATCCCGGACCCCCTTGGCTACCACAACCAGCTGCTGAACCGAATG
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TCCTCGGGCATTGATGCCCTCAGCCACCACAGCCCCAGCGGCTCGTCGGACGCCAGTGGTGGCTTT
GGCATTGCCCTGAGCACCCACGCCAACGGTCTGGACTCGCCGCCTATGTTCGCAGGTGCGGGGCTG
GGAGGCAACCCGTGCCGCAAGAGCTACGAGGACTGTACTAGTGGTATCATGGAGGACTCCGCCAT
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TGGCTACCACTACGGAGTGGCCTCCTGCGAGGCTTGCAAGGCGTTCTTCAAGAGAACCATTCAAGG
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CAGGACAAGCTGTATGCTATGCCTCCCAACGATATCCCCGAGGGAGATATCAAGGCCCTGACCACT
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CCCAGTCTGACACTTGGGGACCAGATGAGCCTGCTGCAGAGTGCCTGGATGGAGATTCTCATCTTG
GGCATCGTGTACCGCTCGCTCCCATACGATGACAAGCTGGCATACGCCGAGGACTATATCATGGAT
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TGCAGGACTATGAGCTGAGTCAGCGCCACGAGGAGCCGCGGAGGGCCGGCAAGCTGCTGCTGACG
CTGCCCCTGCTGAGGCAGACAGCCGCCAAAGCCGTGCAACACTTCTACAGTGTGAAACTGCAGGG
CAAGGTGCCCATGCACAAACTCTTCCTGGAGATGCTGGAGGCCAAGGTGTGA

***Klf4* (NM_010637)**

ATGAGGCAGCCACCTGGCGAGTCTGACATGGCTGTCAGCGACGCTCTGCTCCCGTCCTTCTCCACG
TTCGCGTCCGGCCCGGCGGGAAGGGAGAAGACACTGCGTCCAGCAGGTGCCCCGACTAACCGTTG
GCGTGAGGAACTCTCTCACATGAAGCGACTTCCCCCACTTCCCGGCCGCCCCTACGACCTGGCGGC
GACGGTGGCCACAGACCTGGAGAGTGGCGGAGCTGGTGCAGCTTGCAGCAGTAACAACCCGGCCC
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GCCGGTCCCTAGAGGCCCATTTGAGCGCTGGACCCCAGCTCAGCAACGGCCACCGGCCCAACACA
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CTCAAGGCACACCTGCGAACTCACACAGGCGAGAAACCTTACCACTGTGACTGGGACGGCTGTGG
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ACTTTTAA

***Tfcp2l1* (NM_023755)**

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CAAGATCTGAACACGAAATATGTGAAGAGCATCATCCGTGTCGTTTTCCATGACCGCCGGCTGCAG
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GTTTTTGTGGGACCCATCGAAGAGAGCATCTGCATTCATTCAGGTGCACTGTATCAGCACGGAgTTC
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GAATGAGAGTGGGGACTACTCGGAGCATCTACACTCTGCCAGCTGCCAGATCAAGGTGTTCAAGCC
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CCCTACCAGGCGAACAACACCCCATCCCCAAGCTACAATGGCTCTCCCAACAGCTTTGGCCTCCGT
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TCAGCCTCTATCCAGGATGCACAGCAGTGGCTGCATCGCAACCGCTTCTCACAATTCTGCTGGCTCT
TTGCCAGCTTCTCAGGTGCTGACCTCCTGAAGATGTCCAGAGATGATTTGGTCCAGGTCTGTGGCCC
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ATGTCTGTCAGGAGCTGGAGCAAAACCAACTACCCTTGCCACAGAAGCAGGATGACAGTGGGGAT
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ATCGCCAGCCTGTACAGCATCCCCCCACAGCATATACACCGCGTCTATCGACAGGGTCCCGCTGGC
ATCCACGTGGTGGTAAGCAATGAGATGGTTCAGAATTTCCAAGATGAGTCTTGTTTTATCCTCAGC
ACATTAAAAGCAGAAAGCAATGATGGCTACCACATCATCCTGAAGTGTGGACTCTGA

Table S4: Primers designed for site-directed mutagenesis of ESRRB, KLF4 and TFCP2L1 binding sites.

Targeted site	Forward primer (from 5' to 3') *
ΔKlf4 [-9/-19] (GGGGCGGGGC)	CTGAGGGGCTCGCAGCCCTCcgaattccGCGCGAGGGCGAAGCTTGGCAA
ΔKlf4 [-185/-195] (ACCCCGCCCC)	GCCCCGCCTACCACGTCCGCttgtgaattCCGGCGCGCAGGCCCTGACAT
ΔTfcp2l1 [-390/-404] (CCAGTCAAGCCCGG)	GCCCTCCCGTGCCTCACTgaattcaatcgcgaCCGCCGATCATTGCGATC
ΔEsrrb/Nr5a2 [-538/-548] (TGACCTTGGG)	CCAGGAGCCACAAGCTGTTGaagaattcatGACACCCACGCGCCGGACTC
ΔEsrrb [-870/-880] (CTGAAGGTCA)	CCAGCAGCTCGGGCGGAGGGatgaattcttGGTCTGGGGTGGGTGAGGGT

* Primers are centered on the mutated TFBS and mutated nucleotides are written in lower case.

Table S5: shRNA sequences.

Gene		shRNA name	Targeted sequence (from 5' to 3')	Loop
Esrrb	NM_011934	**Esrrb #1**	GATTCGATGTACATTGAGA	ttcaagaga
Esrrb	NM_011934	**Esrrb #2**	GATCGTCTCGAATCTACTA	ttcaagaga
Klf4	NM_010637	**Klf4 #1**	GGTCATCAGTGTTAGCAAA	ttcaagaga
Klf4	NM_010637	**Klf4 #2**	GGACCTAGACTTTATCCTTTC	ttcaagaga
Tfcp2l1	NM_023755	**Tfcp2l1 #1**	ATCAAAGGACCCTCCAACTGC	ttcaagaga
Tfcp2l1	NM_023755	**Tfcp2l1 #2**	AATACATCAAAGGACCCTCCA	ttcaagaga
		Control	GGACCTAGACTTTATCCTTTC	ttcaagaga