Supplementary Tables

Supplementary Table 1. Primers used to clone LADL plasmids
See attached .xls file.

Supplementary Table 2. Primers and matched plasmids for cloning LADL constructs.

Name of insert	Primers	PCR template	Size (bp)
LADL Anchor Control plasmid			
EF1a	MRP177, MRP 188	Addgene #47457	1237
3XFLAG-dCas9	MRP189, MRP 190	dCas9 plasmid	4300
GS-CIBN	MRP198, MRP 199	Addgene #47457	649
2A-Puro	MRP200, MRP 182	Addgene #62987	681
Empty anchor Control plasmid			
EF1a	MRP036, JV002	Addgene #47457	1237
Puro	JV001, MRP 051	Addgene #62987	681
Empty target Control plasmid			
EF1a	MRP177, MRP 178	Addgene #47457	1247
CRY2PHR	MRP179, MRP 183	Addgene #47457	1700
2A-mCherry	MRP184, MRP 185	CRY2olig mut 2-1	681

Supplementary Table 3. List of gRNA primer sequences

Primer number	gRNA Primer name	gRNA sequence	Backbone plasmid (single clone)	Multiplex
129	*Klf4*_Enh_1_F	CACCGTACATGCAGTAGTACTAAGT	S12.1	**Desert gRNAs (*Klf4*/ *Zfp462*)**
130	*Klf4*_Enh_1_R	AAACACTTAGTACTACTGCATGTAC	S12.1	
135	*Klf4*_Enh_2_F	CACCGTTTGTGTTTTAGTGTAGATT	B1	
136	*Klf4*_Enh_2_R	AAACAATCTACACTAAAACACAAAC	B1	
115	*Zfp462*_Prom_2_F	CACCGTAAAGAAAAGTGTTTATCGA	B2	
116	*Zfp462*_Prom_2_R	AAACTCGATAAACACTTTTCTTTAC	B2	
117	*Zfp462*_Prom_1_F	CACCGAAGTGTTTATCGAGGGAAAG	B3	
118	*Zfp462*_Prom_1_R	AAACCTTTCCCTCGATAAACACTTC	B3	
115	*Zfp462*_Prom_2_F	CACCGTAAAGAAAAGTGTTTATCGA	S12.1	**Promoter only Target plasmid (*Zfp462* only)**
116	*Zfp462*_Prom_2_R	AAACTCGATAAACACTTTTCTTTAC	S12.1	
117	*Zfp462*_Prom_1_F	CACCGAAGTGTTTATCGAGGGAAAG	B1	
118	*Zfp462*_Prom_1_R	AAACCTTTCCCTCGATAAACACTTC	B1	

Supplementary Table 4. List of plasmids with individual gRNAs without soluble CRY2

gRNA in plasmid	gRNA Primer name	BbsI digested plasmid backbone	Targeting region	Genomic feature of target	Refer to
129	*Klf4*_Enh_1_F	S12.1	Engineered Loop Anchor 2	Desert near SE	**Supplementary Figure 2e**
135	*Klf4*_Enh_2_F	B1 (Addgene # 58778)	Engineered Loop Anchor 2	Desert near SE	**Supplementary Figure 2f**
115	*Zfp462*_Prom_2_F	B2 (Addgene # 58779)	Engineered Loop Anchor 1	Desert near *Zfp462* TSS	**Supplementary Figure 2g**
117	*Zfp462*_Prom_1_F	B3 (Addgene # 58780)	Engineered Loop Anchor 1	Desert near *Zfp462* TSS	**Supplementary Figure 2h**

Supplementary Table 5. List of plasmids with multiplexed gRNAs without soluble CRY2

gRNAs in plasmid	gRNA Primer name	BsaI digest plasmid backbone	Targeting region	Multiplex Plasmid name	Refer to
129	*Klf4*_Enh_1_F	S12.1	Desert near SE and Desert near *Zfp462* TSS	Empty bridge control plasmid	**Supplementary Figure 2i**
135	*Klf4*_Enh_2_F				
115	*Zfp462*_Prom_2_F				
117	*Zfp462*_Prom_1_F				

Supplementary Table 6. List of plasmids with multiplexed gRNAs with soluble CRY2

gRNAs in plasmid	gRNA Primer name	BsaI digest plasmid backbone	Targeting region	Multiplex Plasmid name	Refer to
129	*Klf4*_Enh_1_F	S12.1	Desert near SE and Desert near *Zfp462* TSS	LADL Bridge + Target	**Supplementary Figure 2l**
135	*Klf4*_Enh_2_F				
115	*Zfp462*_Prom_2_F				
117	*Zfp462*_Prom_1_F				
115	*Zfp462*_Prom_2_F	S12.1	Desert near *Zfp462* TSS	One-sided guide Control	**Supplementary Figure 2m**
117	*Zfp462*_Prom_1_F				

Supplementary Table 7. List of primers used for RNA qRT-PCR

Name	**Sequence**
Nanog_F_MR137	TGCCTGCAGTTTTTCATCCC
Nanog_R_MR138	TAGAAGAATCAGGGCTGCCTTG
Mouse_GAPDH_F_MR141	GCACAGTCAAGGCCGAGAAT
Mouse_GAPDH_R_MR142	GCCTTCTCCATGGTGGTGAA
Sox2_F_MR143	GCACATGAACGGCTGGAGCAACG
Sox2_R_MR144	TGCTGCGAGTAGGACATGCTGTAGG
*Klf4*_F_MR147	AGACCAGATGCAGTCACAAGTC
*Klf4*_R_MR148	TTTTGCCACAGCCTGCATAG
Oct4_F_MR151	TGTGGACCTCAGGTTGGACT
Oct4_R_MR152	TTTCATGTCCTGGGACTCCTC
MRP213_qPCR_*Zfp462*_F	GCCAACTGATGTTGCCGAGGACAATG
MRP214_qPCR_*Zfp462*_R	CCTGAAGTAGCGTACGCAGAACTTG
MRP215_qPCR_Zhang_dCas9_F	GCACAGCATCAAGAAGAACCTG
MRP216_qPCR_Zhang_dCas9_R	CGTTGCTGAAGATCTCTTGCAG
MRP149_CRY2_qPCR_F	AATGCCTCGACATGTCCATC
MRP150_CRY2_qPCR_F	AGCGCGTTACTGGGTTTTTC
Nestin_Fwd_JB	AGGCCACTGAAAAGTTCCAG
Nestin_Rev_JB	TAAGGGACATCTTGAGGTGTGC

Supplementary Table 8: Summary of external sequencing libraries analyzed in this study
See attached .xls file.

Supplementary Table 9. List of primers used for Chromatin Immunoprecipitation

Primer number	ChIP Primer name	Sequence	Target region
MRP217	MRP217_IP_Down_Y_ED_129to135_F	TGGGCCTACTTAGTACTACTGC	Engineered site at SE
MRP218	MRP218_IP_Down_Y_ED_129to135_R	GCTGGGTAAGTAGCCCTCTAC	Engineered site at SE
MRP221	MRP221_IP_Down_H_ED_115to117_F	AAGCCCCTTTCCCTCGATAAAC	Engineered site at *Zfp462* promoter
MRP222	MRP222_IP_Down_H_ED_115to117_R	ACACTAGGAGGATGGGGATAGTC	Engineered site at *Zfp462* promoter
MRP223	MRP223_IP_H_CTCF_149to155_F	GCTCTATGTTCTAACACCTCTCC	Negative control
MRP224	MRP224_IP_H_CTCF_149to155_R	CGTGCTTGTACACACACACAG	Negative control

Supplementary Table 10. 5C Primer Sequences.
See attached .xls file.

Supplementary Table 11. 5C Primer Genomic Coordinates.
See attached .xls file.

Supplementary Table 12: Summary of mapped 5C sequencing reads
See attached .xls file.

Supplementary Table 13. Fluorescence-labeled oligonucleotide sequences for RNA FISH.
See attached .xls file.