

Supplementary information, Table S6, Key Resources Table

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Antibodies		
Rabbit polyclonal anti-neuron specific beta III Tubulin	Abcam	Cat# ab18207, RRID: AB_444319
Rabbit polyclonal anti-alpha smooth muscle Actin	Abcam	Cat# ab5694, RRID: AB_2223021
Rabbit monoclonal anti-GATA-6 (D61E4)	Cell Signaling Technology	Cat# 5851, RRID: AB_10705521
Mouse monoclonal anti-SSEA1 (MC480)	Abcam	Cat# ab16285, RRID: AB_870663
Mouse monoclonal anti-SSEA4 (MC813)	Abcam	Cat# ab16287, RRID: AB_778073
Mouse monoclonal anti-human-TRA-1-60	Cell Signaling Technology	Cat# 4746, RRID: AB_2119059
Mouse monoclonal anti-human-TRA-1-81	Cell Signaling Technology	Cat# 4745, RRID: AB_2119060
Rabbit polyclonal anti-SOX1	Abcam	Cat# ab87775, RRID: AB_2616563
Rabbit polyclonal anti-Brachyury/Bry	Abcam	Cat# ab20680, RRID: AB_727024
Rabbit polyclonal anti-H3K27ac	Abcam	Cat# ab4729; RRID: AB_2118291
Rabbit polyclonal anti-TBR2 / Eomes	Abcam	Cat# ab23345, RRID: AB_778267
Mouse monoclonal anti-E Cadherin	Abcam	Cat# ab76055, RRID: AB_1310159
Mouse monoclonal anti-Oct-3/4 (C-10)	Santa Cruz Biotechnology	Cat# sc-5279, RRID: AB_628051
Mouse monoclonal anti-Sox-2 (E-4)	Santa Cruz Biotechnology	Cat# sc-365823, RRID: AB_10842165
Rabbit polyclonal anti-human Nanog	PeproTech	Cat# 500-P236, RRID: AB_1268274
Rabbit monoclonal anti-Phospho-Stat3 (Tyr705) (D3A7)	Cell Signaling Technology	Cat# 52075, RRID: AB_2799407
Rabbit monoclonal anti-Stat3 (D3Z2G)	Cell Signaling Technology	Cat# 12640S, RRID: AB_2629499
Rabbit monoclonal anti-GAPDH (D16H11)	Cell Signaling Technology	Cat# 5174, RRID: AB_10622025
Goat anti-Mouse IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor 488	Thermo Fisher Scientific	Cat# A-11001, RRID: AB_2534069
Goat anti-Mouse IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor 594	Thermo Fisher Scientific	Cat# A-11005, RRID: AB_141372
Donkey anti-Rabbit IgG (H+L) Highly Cross-Adsorbed Secondary Antibody, Alexa Fluor 594	Thermo Fisher Scientific	Cat# A-21207, RRID: AB_141637

Donkey anti-Rabbit IgG (H+L) Highly Cross-Adsorbed Secondary Antibody, Alexa Fluor 488	Thermo Fisher Scientific	Cat# A-21206, RRID: AB_2535792
Chemicals, Peptides, and Recombinant Proteins		
CHIR99021	Selleckchem	Cat# S1263
IWR-1-endo	Selleckchem	Cat# S7086
Y-27632	Selleckchem	Cat# S1049
WH-4-023	Selleckchem	Cat# S7565
SB431542	Selleckchem	Cat# S1067
Ruxolitinib (INCB018424)	Selleckchem	Cat# S1378
PD0325901	Selleckchem	Cat# S1036
Recombinant Murine BMP-4	PeproTech	Cat# 315-27
Human/Murine/Rat Activin A (E.Coli)	PeproTech	Cat# 120-14E
Recombinant Human LIF	PeproTech	Cat# 300-05
Recombinant Human FGF-basic (154 a.a.)	PeproTech	Cat# 100-18B
All-Trans Retinoic Acid	PeproTech	Cat# 3027949
Recombinant Human Noggin	PeproTech	Cat# 120-10C
Bovine Serum Albumin	Sigma-Aldrich	Cat# A1470
Ascorbic Acid	Sigma-Aldrich	Cat# A4544
KnockOut Serum Replacement	Thermo Fisher Scientific	Cat# A3181502
Neurobasal™ Medium	Thermo Fisher Scientific	Cat# 21103-049
DMEM/F-12, GlutaMAX™ supplement	Thermo Fisher Scientific	Cat# 10565-018
N-2 Supplement (100 ×)	Thermo Fisher Scientific	Cat# 17502-048
B-27™ Supplement (50 ×), minus vitamin A	Thermo Fisher Scientific	Cat# 12587-010
GlutaMAX™ Supplement	Thermo Fisher Scientific	Cat# 35050-061
MEM Non-Essential Amino Acids Solution (100 ×)	Thermo Fisher Scientific	Cat# 11140-050
2-Mercaptoethanol	Thermo Fisher Scientific	Cat# 21985-023
Penicillin-Streptomycin (10,000 U/mL)	Thermo Fisher Scientific	Cat# 15140-122
Gelatin (0.1% in water)	Stem Cell Technologies	Cat# 07903
Trypsin-EDTA (0.05%), phenol red	Gibco	Cat# 25300120
DMEM, high glucose, no glutamine	Gibco	Cat# 11960-044
Fetal bovine serum (FBS)	Gibco	Cat# 16000-044
Accutase cell dissociation reagent	Gibco	Cat# A11105-01
TrypLE™ Express	Gibco	Cat# 12605010
Dulbecco's phosphate-buffered saline (DPBS)	Gibco	Cat# C14190500CP
Critical Commercial Assays		
KAPA Hyper Prep Kits	KAPA Biosystems	Cat# KK8054
RNeasy Mini Kit	QIAGEN	Cat# 74106
Globin-Zero Gold rRNA Removal Kit	Illumina	Cat# GZG1224
NEBNext® Ultra™ Directional RNA Library Prep Kit for Illumina®	New England Biolabs	Cat# E7760
NEXTflex™ ChIP-Seq Kit	Bioo Scientific	Cat# NOVA-5143-02
RNAprep pure Cell / Bacteria Kit	TIANGEN	Cat# DP430
5 × All-In-One RT Master Mix	ABM	Cat# G490
TIANamp Genomic DNA Kit	TIANGEN	Cat# DP304
Rapid Giemsa staining kit	BBi Life Sciences	Cat# E202FA0001
Gel & PCR Clean Up Kit	OMEGA	Cat# D2000-02
Lipofectamine™ 3000 Transfection Kit	Invitrogen	Cat# 2173193

Lipofectamine [™] Stem Transfection Reagent	Invitrogen	Cat# STEM00008
Endo-free Plasmid Mini Kit	OMEGA	Cat# D6950-02B
Bradford Protein Assay Kit	BIO-RED	Cat# 5000201
2 × RealStar Green Power Mixture	GenStar	Cat# A311-05
Cells-to-cDNA [™] II Kit	Invitrogen	Cat# AM8723
Deposited Data		
Pig preimplantation embryos and pgEpiSCs scRNA-seq data	This paper	CRA003960
Whole genome resequencing of pgEpiSCs	This paper	CRA003960
Raw and analyzed Hi-C data for 16 libraries in pgEpiSCs and 16 libraries in pEFs	This paper	CRA003960
Raw RNA-seq data for 4 libraries in pgEpiSCs and 2 libraries in pEFs	This paper	CRA003960
H3K27ac ChIP-seq for 2 libraries in pgEpiSCs and 2 libraries in pEFs	This paper	CRA003960
ATAC-seq for 3 libraries in pgEpiSCs and 2 libraries in pEFs	This paper	CRA003960
Human ESCs Hi-C data	1,2	GSE52457, GSE105028
Human dermal fibroblasts Hi-C data	3	GSE123552
Mouse ESCs Hi-C data	4,5	GSE96107, GSE124342
Mouse embryonic fibroblasts Hi-C data	6,7	GSE113339
Human ESCs RNA-seq data	8	GSE69692
Human dermal fibroblasts RNA-seq data	9	GSE78670
Mouse ESCs RNA-seq data	10	GSE121171
Mouse embryonic fibroblasts RNA-seq data	6	GSE113431
Human formative PSCs, mouse naive, formative and primed PSCs RNA-seq data	11	GSE131556
Human naive and conventional PSCs RNA-seq data	12	E-MTAB-5674
Human naive and conventional PSCs RNA-seq data	8	GSE69692
pEPSC_Gao RNA-seq data	13	E-MTAB-7253
pESC_Choi RNA-seq data	14	GSE120031
piPSC_Secher RNA-seq data	15	GSE92889
pESCLC_Yuan and piPSC_Yuan RNA-seq data	16	GSE126150
piPSC_Shi RNA-seq data	17	GSE143484
piPSC_Xu RNA-seq data	18	GSE141935
Experimental Models: Cell Lines		
1-pgEpiSCs	This paper	N/A
2-pgEpiSCs	This paper	N/A
3-pgEpiSCs	This paper	N/A
4-pgEpiSCs	This paper	N/A
PEF	This paper	N/A
MEF	This paper	N/A
Experimental Models: Organisms		
CD-1 [®] (ICR) IGS Mice	Vital River	201
BALB/c Nude Mice	Vital River	401

BAMA pigs	Beijing Farm Animal Research Center	N/A
Nongda pigs	CAU Experimental Miniature Pig Farm	N/A
DLY pigs	YAU/NEAU Experimental Pig Farm	N/A
Oligonucleotides		
TSO primer: AAGCAGTGGTATCAACGCAGAGTACATrGrG+G	This paper	N/A
ISPCR: AAGCAGTGGTATCAACGCAGAGT	This paper	N/A
3'-P2: GTGACTGGAGTTCAGACGTGTGCTCTTCCGATC	This paper	N/A
short universal primer: AATGATACGGCGACCACCGAGATCTACACTCTTT CCCTACACGAC	This paper	N/A
illunima-QP2: CAAGCAGAAGACGGCATACGA	This paper	N/A
<i>POU5F1</i> : Forward: CAAACTGAGGTGCCTGCCCTTC Reverse: ATTGAACTTCACCTTCCCTCCAACC	This paper	N/A
<i>NANOG</i> : Forward: CATCTGCTGAGACCCTCGAC Reverse: GGGCTTGTGGAAGAATCAGG	This paper	N/A
<i>SOX2</i> : Forward: CATCAACGGTACACTGCCTCTC Reverse: ACTCTCCTCCCATTTCCTCTTT	This paper	N/A
<i>REX1(ZFP42)</i> : Forward: GGGATCACGTGTGTGCAGAA Reverse: TTCCTGCGACAGCCTTCAAA	This paper	N/A
<i>CDH1</i> : Forward: GACTTCTGCCAGAGGAACCC Reverse: CACTGGCCCCATGTGTTAGT	This paper	N/A
<i>IGF2</i> : Forward: CGTGCTGCTATGCTGCTTAC Reverse: AAGCAGCACTCTTCCACGAT	This paper	N/A
<i>SNAI2</i> : Forward: CCCACACCCTACCTTGTGTC Reverse: TGACATCCGAGTGTGTCTGC	This paper	N/A
<i>SRC</i> : Forward: GCCAACATCCTGGTTGGAGA Reverse: ATCCCAAAGGACCACACGTC	This paper	N/A
<i>WNT5A</i> : Forward: CGCGAAGACAGGCATCAAAG Reverse: CCTATCTGCATGACCCTGCC	This paper	N/A

GATA6: Forward: CACTACTTGTGCAACCGCTG Reverse: TTCTGCGGCTTTATGAGGGG	This paper	N/A
HAND1: Forward: TGCGAGTGCATACCTTCTGT Reverse: AGGCCCTGAGGGGAGTTTAT	This paper	N/A
PAX6: Forward: TGTCCAACGGATGTGTGAGT Reverse: TCTGTCTCGGATTTCCCAA	This paper	N/A
CDH2: Forward: GCCTCAAGCCAACCTTACCT Reverse: AGCTCTTGAGGAAAAGGCCC	This paper	N/A
ID2: Forward: TCGCACCCCACTATTGTCAG Reverse: TTCAGAAGCCTGCAAGGACA	This paper	N/A
ID3: Forward: CATCTTCCCATCCAGACAGCC Reverse: GTCAAGTGGGCACGACAAAG	This paper	N/A
BMP2: Forward: GTCTTTCGGGAGCAGACACA Reverse: GTCACCAACCTGGTGTCCAA	This paper	N/A
EOMES: Forward: ACTCCCATGGACCTCCAGAA Reverse: TCGCTTACAAGCACTGGTGT	This paper	N/A
T: Forward: GAAGTACGTGAACGGGGAGT Reverse: CACGATGTGGATTGAGGCT	This paper	N/A
LIN28A: Forward: TGCCGGCATCTGTAAATGGT Reverse: ACTCTGGTGCACAAAGACGT	This paper	N/A
C-MYC: Forward: ATCCAAGACCACCACCACTG Reverse: GTTCACAGCAACATTCAGGTAGA	This paper	N/A
ETV4: Forward: AGAACCGGCCAGCTATGAAC Reverse: ATTGTCCGGGAAAGCCAGAG	This paper	N/A
ETV5: Forward: TCAGCACATGGGTTCAGTC Reverse: CCTTCATGGCTGCTGGAGAA	This paper	N/A
BMP4: Forward: TTCATTTTAGGAGCCATTCTGTAGT Reverse: TCCTAGCAGGACTTGGCATAAT	This paper	N/A
EF-1α: Forward: AATGCGGTGGGATCGACAAA Reverse: CACGCTCACGTTGAGCCTTT	This paper	N/A

<i>TYR</i> gene sgRNA targeting sequence: Forward: ACCGACCTCAGTTCCCCTTCACCG Reverse: AAACCGGTGAAGGGGAACTGAGGT	This paper	N/A
<i>TYR</i> gene mutant site test primer: Forward: CTGGACTTTCCAGACTTCCG Reverse: GTGCAGTTGGGTCCCTGAAA	This paper	N/A
<i>GFP</i> test primer Forward: CAACACCCGCATCGAGAAGT Reverse: ACCACGAAGCTGTAGTAGCC	This paper	N/A
<i>NANOG</i> knock-in 3' ARM test primer Forward: GCAACCTCCCCTTCTACGAG Reverse: GTGAAGCACACGGTAGGGTA	This paper	N/A
<i>NANOG</i> knock-in 5' ARM test primer Forward: TGTCCATTGCTGAAGCATGTAAT Reverse: GAAGTTAGTAGCTCCGCTTCCTG	This paper	N/A
Recombinant DNA		
pGL3-U6-gRNA-EGFP	Xingxu, Huang's Lab	N/A
pCMV_AncBE4max	Xingxu, Huang's Lab	N/A
PB-CMV-EF1A-GFP-NLS	This paper	N/A
Nanog-tdTomato-donor vector	Our Laboratory	N/A
Software and Algorithms		
Snap Gene software	Insightful Science	https://www.snapgene.com
CRISPR sgRNA Design Tool	19	https://www.genscript.com/gRNA-design-tool
STAR version 2.7.1a	20	https://github.com/alexdobin/STAR
Subread version 1.6.4	21	https://sourceforge.net/projects/subread
SAMtools version 1.9	22	http://samtools.sourceforge.net
UMI-tools	23	https://github.com/CBGT/Oxford/UMI-tools
R version 3.6.0	N/A	https://www.R-project.org
Rstudio	N/A	https://rstudio.com
Seurat (version 3.0.0)	24	https://satijalab.org/seurat
STAR v2.6.0c	20	https://github.com/alexdobin/STAR/releases/tag/2.6.0c
Kallisto v0.44.0	25	http://pachterlab.github.io/kallisto/releases/2018/01/29/v0.44.0

DESeq2 v1.28.1	26	https://bioconductor.org/packages/release/bioc/html/DESeq2
BWA v0.7.15	27	https://github.com/lh3/bwa/releases/tag/v0.7.15
SAMtools v0.1.19	22	https://github.com/samtools/samtools/tree/0.1.19
SICER v1.1	28	https://github.com/dariober/SICERpy
Juicer	29	https://github.com/aidenlab/juicer
quantile algorithm	30	https://bioconductor.org/packages/release/bioc/html/bnbc
HiCRep	31	https://www.bioconductor.org/packages/release/bioc/html/hicrep
miniMDS	32	https://github.com/seqcode/miniMDS
PSYCHIC	33	https://github.com/dhkron/PSYCHIC
ROSE algorithm v0.1	34,35	https://github.com/rakarnik/ROSE
HiCCUPS	36	https://github.com/aidenlab/juicer/wiki/HiCCUPS
Trim_galore	DOI:10.5281/zenodo.5127898	https://github.com/FelixKrueger/TrimGalore
Bowtie2	37	https://github.com/BenLangmead/bowtie2
GATK	38	https://github.com/broadinstitute/gatk
ANNOVAR	39	https://github.com/WGLab/doc-ANNOVAR
MACS2	40	https://pypi.org/project/MACS2/
HTSeq	41	https://github.com/htseq/htseq

edgeR	42	https://bioconductor.org/packages/release/bioc/html/edgeR.html
MEME	43	https://meme-suite.org/meme/
PyMOL	DeLano, W.L. (2002) The PyMol molecular graphics system	https://pymol.org/2/
BEDtools2	44	https://github.com/arq5x/bedtools2
IGV v2.6.0	45	http://www.igv.org
Metascape	46	https://metascape.org
Pheatmap	N/A	https://cran.r-project.org/web/packages/pheatmap/index
ggplot2	N/A	https://ggplot2.tidyverse.org
WGCNA v1.68	47	https://horvath.genetics.ucla.edu/html/CoexpressionNetwork/Rpackages/WGCNA
Cytoscape	48	https://cytoscape.org
AUCell v1.5.2	49	https://bioconductor.org/packages/AUCell
Cutadapt v3.0	50	https://cutadapt.readthedocs.io
GraphPad Prism 8	GraphPad Prism	https://www.graphpad.com
monocle3 v1.0.0	51	https://cole-trapnell-lab.github.io/monocle3
velocity	52	http://velocityto.org
DomainCaller	53	https://github.com/XiaoTaoWang/domaincaller

Reference:

- 1 Dixon, J. R. *et al.* Chromatin architecture reorganization during stem cell differentiation. *Nature* **518**, 331-336 (2015).
- 2 Lyu, X., Rowley, M. J. & Corces, V. G. Architectural Proteins and Pluripotency Factors Cooperate to Orchestrate the Transcriptional Response of hESCs to Temperature Stress. *Mol. Cell* **71**, 940-955 e947 (2018).
- 3 Nir, G. *et al.* Walking along chromosomes with super-resolution imaging, contact maps, and integrative modeling. *PLoS Genet.* **14**, e1007872 (2018).
- 4 Bonev, B. *et al.* Multiscale 3D Genome Rewiring during Mouse Neural Development. *Cell* **171**, 557-572 e524 (2017).
- 5 McLaughlin, K. *et al.* DNA Methylation Directs Polycomb-Dependent 3D Genome Re-organization in Naive Pluripotency. *Cell Rep.* **29**, 1974-1985 e1976 (2019).
- 6 Di Giammartino, D. C. *et al.* KLF4 is involved in the organization and regulation of pluripotency-associated three-dimensional enhancer networks. *Nat. Cell Biol.* **21**, 1179-1190 (2019).
- 7 Colognori, D., Sunwoo, H., Kriz, A. J., Wang, C. Y. & Lee, J. T. Xist Deletional Analysis Reveals an Interdependency between Xist RNA and Polycomb Complexes for Spreading along the Inactive X. *Mol. Cell* **74**, 101-117 e110 (2019).
- 8 Ji, X. *et al.* 3D Chromosome Regulatory Landscape of Human Pluripotent Cells. *Cell Stem Cell* **18**, 262-275 (2016).
- 9 Consortium, E. P. An integrated encyclopedia of DNA elements in the human genome. *Nature* **489**, 57-74 (2012).
- 10 Shukla, R. *et al.* Activation of transcription factor circuitry in 2i-induced ground state pluripotency is independent of repressive global epigenetic landscapes. *Nucleic Acids Res.* **48**, 7748-7766 (2020).
- 11 Kinoshita, M. *et al.* Capture of Mouse and Human Stem Cells with Features of Formative Pluripotency. *Cell Stem Cell* **28**, 453-471 e458 (2021).
- 12 Guo, G. *et al.* Epigenetic resetting of human pluripotency. *Development* **144**, 2748-2763 (2017).
- 13 Gao, X. *et al.* Establishment of porcine and human expanded potential stem cells. *Nat. Cell Biol.* **21**, 687-699 (2019).
- 14 Choi, K. H. *et al.* Chemically Defined Media Can Maintain Pig Pluripotency Network In Vitro. *Stem Cell Reports* **13**, 221-234 (2019).
- 15 Secher, J. O. *et al.* Systematic in vitro and in vivo characterization of Leukemia-inhibiting factor- and Fibroblast growth factor-derived porcine induced pluripotent stem cells. *Mol. Reprod. Dev.* **84**, 229-245 (2017).
- 16 Yuan, Y. *et al.* A six-inhibitor culture medium for improving naive-type pluripotency of porcine pluripotent stem cells. *Cell Death Discov.* **5**, 104 (2019).
- 17 Shi, B. *et al.* IRF-1 expressed in the inner cell mass of the porcine early blastocyst enhances the pluripotency of induced pluripotent stem cells. *Stem Cell. Res. Ther.* **11**, 505 (2020).
- 18 Xu, J. *et al.* A cytokine screen using CRISPR-Cas9 knock-in reporter pig iPS cells reveals that Activin A regulates NANOG. *Stem Cell. Res. Ther.* **11**, 67 (2020).
- 19 Labun, K. *et al.* CHOPCHOP v3: expanding the CRISPR web toolbox beyond genome editing. *Nucleic Acids Res.* **47**, W171-W174 (2019).
- 20 Dobin, A. *et al.* STAR: ultrafast universal RNA-seq aligner. *Bioinformatics* **29**, 15-21 (2013).
- 21 Liao, Y., Smyth, G. K. & Shi, W. The Subread aligner: fast, accurate and scalable read mapping by seed-and-vote. *Nucleic Acids Res.* **41**, e108 (2013).

- 22 Li, H. *et al.* The Sequence Alignment/Map format and SAMtools. *Bioinformatics* **25**, 2078-2079 (2009).
- 23 Smith, T., Heger, A. & Sudbery, I. UMI-tools: modeling sequencing errors in Unique Molecular Identifiers to improve quantification accuracy. *Genome Res.* **27**, 491-499 (2017).
- 24 Stuart, T. *et al.* Comprehensive Integration of Single-Cell Data. *Cell* **177**, 1888-1902 e1821 (2019).
- 25 Bray, N. L., Pimentel, H., Melsted, P. & Pachter, L. Near-optimal probabilistic RNA-seq quantification. *Nat. Biotechnol.* **34**, 525-527 (2016).
- 26 Love, M. I., Huber, W. & Anders, S. Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2. *Genome Biol.* **15**, 550 (2014).
- 27 Li, H. & Durbin, R. Fast and accurate short read alignment with Burrows-Wheeler transform. *Bioinformatics* **25**, 1754-1760 (2009).
- 28 Zang, C. *et al.* A clustering approach for identification of enriched domains from histone modification ChIP-Seq data. *Bioinformatics* **25**, 1952-1958 (2009).
- 29 Durand, N. C. *et al.* Juicer Provides a One-Click System for Analyzing Loop-Resolution Hi-C Experiments. *Cell Syst.* **3**, 95-98 (2016).
- 30 Fletez-Brant, K., Qiu, Y., Gorkin, D. U., Hu, M. & Hansen, K. D. Removing unwanted variation between samples in Hi-C experiments. *bioRxiv*, 214361 (2021).
- 31 Yang, T. *et al.* HiCRep: assessing the reproducibility of Hi-C data using a stratum-adjusted correlation coefficient. *Genome Res.* **27**, 1939-1949 (2017).
- 32 Rieber, L. & Mahony, S. miniMDS: 3D structural inference from high-resolution Hi-C data. *Bioinformatics* **33**, i261-i266 (2017).
- 33 Ron, G., Globerson, Y., Moran, D. & Kaplan, T. Promoter-enhancer interactions identified from Hi-C data using probabilistic models and hierarchical topological domains. *Nat. Commun.* **8**, 2237 (2017).
- 34 Loven, J. *et al.* Selective inhibition of tumor oncogenes by disruption of super-enhancers. *Cell* **153**, 320-334 (2013).
- 35 Whyte, W. A. *et al.* Master transcription factors and mediator establish super-enhancers at key cell identity genes. *Cell* **153**, 307-319 (2013).
- 36 Rao, S. S. *et al.* A 3D map of the human genome at kilobase resolution reveals principles of chromatin looping. *Cell* **159**, 1665-1680 (2014).
- 37 Langmead, B. & Salzberg, S. L. Fast gapped-read alignment with Bowtie 2. *Nat. Methods* **9**, 357-359 (2012).
- 38 Van der Auwera, G. A. *et al.* From FastQ data to high confidence variant calls: the Genome Analysis Toolkit best practices pipeline. *Curr Protoc Bioinformatics* **43**, 11.10.11-11.10.33 (2013).
- 39 Wang, K., Li, M. & Hakonarson, H. ANNOVAR: functional annotation of genetic variants from high-throughput sequencing data. *Nucleic Acids Res.* **38**, e164 (2010).
- 40 Feng, J., Liu, T., Qin, B., Zhang, Y. & Liu, X. S. Identifying ChIP-seq enrichment using MACS. *Nat. Protoc.* **7**, 1728-1740 (2012).
- 41 Anders, S., Pyl, P. T. & Huber, W. HTSeq--a Python framework to work with high-throughput sequencing data. *Bioinformatics* **31**, 166-169 (2015).
- 42 Robinson, M. D., McCarthy, D. J. & Smyth, G. K. edgeR: a Bioconductor package for differential expression analysis of digital gene expression data. *Bioinformatics* **26**, 139-140 (2010).

- 43 Bailey, T. L., Johnson, J., Grant, C. E. & Noble, W. S. The MEME Suite. *Nucleic Acids Res.* **43**, W39-49 (2015).
- 44 Quinlan, A. R. BEDTools: The Swiss-Army Tool for Genome Feature Analysis. *Curr Protoc Bioinformatics* **47**, 11.12.11-34 (2014).
- 45 Thorvaldsdóttir, H., Robinson, J. T. & Mesirov, J. P. Integrative Genomics Viewer (IGV): high-performance genomics data visualization and exploration. *Brief Bioinform* **14**, 178-192 (2013).
- 46 Zhou, Y. *et al.* Metascape provides a biologist-oriented resource for the analysis of systems-level datasets. *Nat. Commun.* **10**, 1523 (2019).
- 47 Langfelder, P. & Horvath, S. WGCNA: an R package for weighted correlation network analysis. *BMC Bioinformatics* **9**, 559 (2008).
- 48 Shannon, P. *et al.* Cytoscape: a software environment for integrated models of biomolecular interaction networks. *Genome Res.* **13**, 2498-2504 (2003).
- 49 Aibar, S. *et al.* SCENIC: single-cell regulatory network inference and clustering. *Nat. Methods* **14**, 1083-1086 (2017).
- 50 Martin, M. Cutadapt removes adapter sequences from high-throughput sequencing reads. *EMBnet J.* **17**, 10 (2011).
- 51 Trapnell, C. *et al.* The dynamics and regulators of cell fate decisions are revealed by pseudotemporal ordering of single cells. *Nat. Biotechnol.* **32**, 381-386 (2014).
- 52 La Manno, G. *et al.* RNA velocity of single cells. *Nature* **560**, 494-498 (2018).
- 53 Dixon, J. R. *et al.* Topological domains in mammalian genomes identified by analysis of chromatin interactions. *Nature* **485**, 376-380 (2012).